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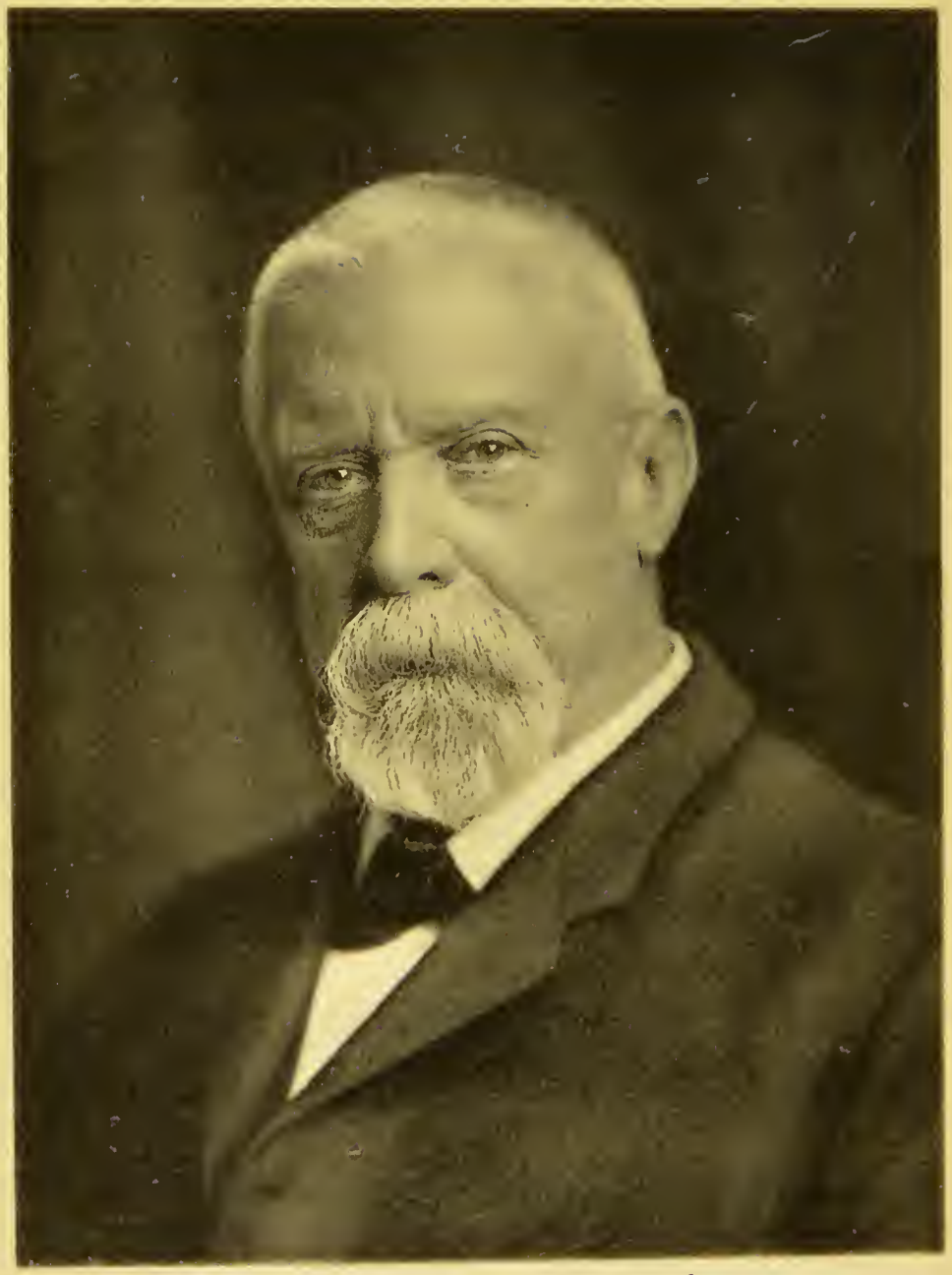
STUDIES IN RABIES

"A man is the son of his own deeds."



Most respectfully,
Nathaniel Garland Keirle.

SCHOOL OF MEDICINE,
UNIVERSITY OF LEEDS.

STUDIES IN RABIES

COLLECTED WRITINGS OF

NATHANIEL GARLAND KEIRLE

A. M., M. D., D. Sc.

Professor of Medical Jurisprudence and Emeritus Professor of Pathology
College of Physicians and Surgeons
Director of the Pasteur Institute, Baltimore, Maryland

WITH AN INTRODUCTION BY
WILLIAM H. WELCH
AND
A BIOGRAPHICAL SKETCH BY
HARRY FRIEDENWALD

Testimonial Edition

BALTIMORE
1909

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Address

to

Dr. Nathaniel Garland Keirle

The undersigned committee publishes this collection of your writings on rabies both for their intrinsic worth and as a mark of the esteem and admiration of a large number of your friends and colleagues whose names are given below.

Your work as a teacher, the scientific stamp of your studies and publications, but most of all your painstaking and successful labors in the preventative treatment of rabies have merited the highest approbation. Your care and accuracy, your untiring persistence and your unwillingness to accept conclusions until thoroughly proved have characterized you as a true scholar and an example of devotion to science. You have not been spared disappointment and you have suffered the greatest of sorrows, but you have borne them with heroic fortitude. Your friends have shared them with you as they likewise take pleasure in your labors and success. For them all, we express the wish for your continued health, vigor and strength steadfastly to pursue your beneficent work.

In presenting you with your writings in this volume, we feel that in honoring you we are showing honor to a true physician, a real scholar, a rare, cultured, and noble man.

Harry Friedenwald
John Wesley Chambers
Archibald E. Harrison
Committee

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NOTE.—The editors desire to express their thanks to the publishers of the *Twentieth Century Practice of Medicine, Maryland Medical Journal, Medical Record, Medical News,* and *New York Medical Journal* for their kind permission to reprint the articles contained in this book.

INTRODUCTION.

By William H. Welch, M. D., LL. D.

It gives me much pleasure to comply with the request to contribute a few introductory lines to this volume of collected papers on rabies by my old and valued friend, Professor Nathaniel G. Keirle. Our acquaintance, which soon grew into cordial friendship, dates from my first coming to Baltimore to live in 1885. For many years before this Dr. Keirle had been actively engaged in making post-mortem examinations and was already recognized as a good student and teacher of pathological anatomy and an authority in legal medicine. We were drawn together by similarity of pursuit and of interest, and I recall with especial satisfaction his frequent visits to my laboratory and his keen and intelligent interest in the work there, particularly in all that related to the attractive fields which had been opened to exploration by the discoveries of Pasteur and of Koch.

Largely by his personal study and efforts he became familiar with the new bacteriological

methods, and undertook investigations which demonstrated genuine scientific ability. I was not a little surprised to learn that he had quietly and patiently repeated the fundamental experiments of Pasteur on rabies and that he had in his possession a fixed virus secured by successive passages through rabbits during a period of two years, and that this virus was in no respect inferior in its quality and efficacy to that in use at the Pasteur Institute in Paris.

The establishment of the Pasteur Institute in connection with the College of Physicians and Surgeons and the City Hospital of Baltimore was due very largely to the efforts of Dr. Keirle, assisted in the early days by the excellent collaboration of Dr. John Ruhräh. As the head of this Institute Dr. Keirle has rendered very important services to the community and has brought the work of the Institute to the highest standard of efficiency in the saving of many lives from the most fatal and dreaded of diseases.

With relatively few advantages of training, save those of his own making, Dr. Keirle has won the high esteem of his professional colleagues by his solid attainments, by his genuinely scientific spirit, by his loyalty to the best ideals

of the profession, by his quiet, unobtrusive but effective work through many years in behalf of patients, students, colleagues and the public, and by noble and winning traits of character. This volume relating to one field of his work is intended as an expression, although an inadequate one, of the respect, admiration and friendship of his colleagues.

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BIOGRAPHICAL SKETCH OF DR. KEIRLE.

The author of this book, whose great services to his profession a number of his colleagues and pupils desire to honor, was born in Baltimore, October 10, 1833.

He is the son of the late Matthew M. Keirle of Baltimore and of Sarah Jacobs Garland of Danvers, Massachusetts. On his mother's side he was the grandson of Nathaniel Garland and his wife Lydia Jacobs. His great grandfather was Benjamin Jacobs, born in Danvers, Massachusetts, March, 1742, who, as lieutenant in Colonel Pickering's regiment, marched to Lexington on April 19, 1775.

His paternal grandfather, John Washington Keirle, was born in 1777. In 1796 he married Ann Murfin and established himself in Baltimore as a successful shoe merchant. The couple had three sons, the eldest being Matthew Murfin Keirle, born December 5, 1798. John Washington Keirle lost his life on the steamer

Lexington, which was burned on Long Island Sound, January 13, 1840.

Matthew was married to Sarah Jacobs Garland and had three children, the eldest being Nathaniel Garland Keirle, the subject of this sketch. Another son, born later, died in early infancy, and a sister, Martha Garland Keirle, was married to a Mr. Patterson and died of consumption in 1880, in her forty-sixth year.

Dr. Keirle's mother, becoming ill with consumption, was taken by her husband to Orange Court House, Virginia, in the hope of relieving her condition. Instead, the husband contracted typhoid fever and died, July 8, 1839, aged forty years; his wife's death followed on September 27, 1839, when she was but thirty years of age, and young Nathaniel scarcely six years. His grandfather's death following soon after, he was taken in charge by his grandmother Keirle and some aunts. He was reared a Baptist, attending the Seventh Baptist Church on the southeast corner of Lombard and Sharp Streets.

He was sent to several private schools in his early youth, and later to St. Mary's Seminary, now St. Mary's College, on Paca Street and Druid Hill Avenue. One of his teachers at this

school is still living, and an old physician, Dr. Felix Jenkins. From this school he was sent to public school No. 6, then on Ross Street, now Druid Hill Avenue, near Biddle Street. His principal was Mr. Creery. He was then passed to the High School, now the City College, and here one of his teachers was the late Judge Duffy. After spending a short time at this school, he entered Dickinson College, passed through the preparatory and collegiate departments, spending five years at Carlisle, and graduating second in his class in 1855. Having taken his A. B. degree, he returned to Baltimore. Here he visited one of the most prominent Baltimore lawyers with the intention of taking up the study of law. The lawyer asked him his age, and on receiving the answer that he was then twenty-two, said: "You are too old to study law." In speaking of the occurrence, Dr. Keirle remarked that he was not bad enough to enter the ministry, so there was nothing left for him to do but to study medicine, though medicine had no attraction whatever for him. He became an office student of Dr. Miltenberger and remained under his preceptorship for two years, and at the same

time attended lectures at the University of Maryland. Two of his classmates are living and are well known to the Baltimore profession, Dr. Samuel C. Chew and Dr. Edward F. Milholland. After graduation, he became resident physician at the Baltimore Almshouse, where he spent five years. When Bay View Asylum was first opened, and the almshouse transferred from the western part of the city to the eastern, he moved with the institution. During this period he became, for a short time, chief resident physician in the Baltimore Infirmary, but soon resigned and returned to the almshouse. Here he worked with Dr. George G. Fernandis, then visiting physician, "whose instruction and example taught (him) how to study and observe." Towards the end of his period of service in this institution, a very severe epidemic of typhus fever broke out in the almshouse, many patients died, and the epidemic gave him the opportunity of studying carefully and of making a large number of post-mortem examinations of this very virulent disease. For his meritorious and efficient services during this epidemic, he was awarded a gold medal and certificate by the trustees and the Mayor of

Baltimore City. During his period of service in the almshouse, Dr. Keirle became especially interested in pathology and performed a large number of post-mortem examinations.

Leaving the almshouse he took up for a short time the practice of a friend near Gettysburg. After the battle of Gettysburg, he served the sick and wounded in the hospital (in the Literary College) at Gettysburg. Here he saw much hospital gangrene, and he himself became quite ill while on duty. He therefore returned to Baltimore; his friends regarded his condition as very serious; his trouble was pleurisy, but tuberculosis was suspected, and several months elapsed before he was able again to undertake work.

When he recovered his health, he opened an office on West Franklin Street. For a while he took up work in dermatology and venereal diseases in connection with the Special Dispensary, then located at the northeast corner of Saratoga and North Streets. Among those working in this dispensary at that time were Drs. Tiffany, Chew, Coskery, Atkinson, and Wm. G. Harrison, Jr. Dr. Keirle also acted as registrar at the dispensary.

In March, 1881, Dr. Coskery secured for him

the position of physician in charge at the City Hospital Dispensary. He was appointed soon after Demonstrator and later Lecturer on Pathology and Medical Jurisprudence. In 1894 he was elected Professor in these departments. He resigned the chair of Pathology in 1902, continuing to hold the chair of Medical Jurisprudence.

At the same time Dr. Keirle was as much interested in microscopic pathology as in macroscopic, and his services were frequently called upon by the physicians and surgeons in the city. His observation was accurate and his knowledge extensive. Great confidence was therefore placed upon his opinions concerning the nature of any morbid process or tissue.

For many years Dr. Keirle has also held the position of medical examiner and post-mortem physician for the City of Baltimore. His unsurpassed attainments in medical jurisprudence have been frequently drawn upon in this work, and especially when called upon as expert witness in our courts.

During this period the post-mortems which were performed by him were carefully recorded, and he now possesses a record of over two

thousand cases, while the total number of post-mortems which he conducted numbers over three thousand.

Dr. Keirle has not been interested only in the pathology of the deadhouse. His experimental investigations have been quite extensive. They were especially directed to the study of pigeon and chicken diphtheria, of rabbit septicæmia, and of rabies in dogs, mice, rabbits, and other animals. Indeed, it is in this department that his life's work has been done. Since the opening of the Pasteur Institute he has been its director. The record of this work will be found in this volume, but the good that he has accomplished and the lives that he has saved cannot be estimated.

His work reflects the honesty of a true student of science. It is characterized by the most punctilious accuracy; just as he cannot bear to see a bottle or an instrument out of its place, or any form of disorder even in the slightest degree in his laboratory or in his animal room, so in all his work there is the greatest precision. And this also distinguishes his daily life. For years he has left his home at 1419 West Lexington Street at a definite time, has come to his

laboratory at the same hour, and has attended to every detail in the same order, day after day, for many years, without a single interruption, without a day's holiday; he was not kept away even by sorrow and deaths.

As he did not enter upon the study of medicine from love of the profession, and as he never became fond of medical practice, he withdrew from general practice many years ago, but his wide knowledge of medicine has stood him in good stead in the treatment of the large number of those whom he has had under his care in the Pasteur Institute.

This sketch would not be complete without reference to the sad history of his domestic life. Dr. Keirle was married January 5, 1870, to Mary Elizabeth Jones; she was the only child of Wrightson Jones, Jr., and Melinda Jeanette Jones, and was born October 16, 1843, at St. Michaels, Talbot County, Maryland. The issue of this marriage were Mary Garland Keirle, born October 21, 1870; Nathaniel Garland Keirle, Jr., born June 24, 1874, and Martha Jones Keirle, born April 13, 1877.

His eldest child, Mary Garland Keirle, died of malignant diphtheria, October 15, 1880, aged

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almost ten. On June 8, 1882, his wife died of pulmonary consumption. His daughter, Martha Jones, for many years an invalid in consequence of scarlet fever, died of Bright's disease, June 19, 1893, aged sixteen years. His son, Nathaniel Garland, a brilliant boy and a devoted son, who had followed his father's footsteps in the study of medicine, had graduated with the highest honors at the College of Physicians and Surgeons in 1899, had distinguished himself as resident physician at the Baltimore City Hospital, at the Hebrew Hospital, and at the Bay View Asylum of Baltimore City, who had studied diligently here and abroad, and had been assisting his father in the work of the Pasteur Institute, died on January 5, 1908, of pneumonia, aged thirty-three and one-half years.

Although Dr. Keirle has reached a time of life when many show the weaknesses of age, he has retained all the physical and mental vigor of his middle life. He has enjoyed good health —in no slight measure because of the regularity of his habits and his moderation in all things. His memory is as accurate as ever. But no quality stands out more prominently than his unfailing good humor and his keen wit. They creep

out at all times, whether in conversation with his friends, on the witness stand, in the lecture hall or in an after-dinner speech. Neither age nor sorrow has dimmed the brilliancy of his wit or embittered his genial good humor. Both are pervaded by the same kind, benign and tender spirit which has won for him the affection and the love of his patients, his pupils, his assistants and his colleagues.

HARRY FRIEDENWALD.

June 7, 1909.

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THE BACILLUS OF RABBIT SEPTICÆMIA OBTAINED FROM THE MEDULLA OBLONGATA OF A SUPPOSED RABID DOG.

In the course of an investigation into the subject of rabies, undertaken last November, it became necessary, for the purpose of control experiments, to use a number of dogs, and one object of these controls being the determination as to whether any other disease than rabies could give rise to like signs and symptoms, it was requisite to use sick dogs; therefore the dogs used had died or been killed because of suspected rabies. The bacteriological developments of dog number 17 are noteworthy. This dog was a yellow cur, weight about 20 pounds, shot and his skull crushed on the 21st of last September. He had attempted to bite a number of persons; did bite other dogs, took refuge in a stable and bit a horse.

Post-mortem examination on the 22nd of September, 1893.

Inspection—Skull crushed and brain torn;

mouth pigmented; cheeks and under surface of tongue bluish vascularity; bits of coal and splinters in mouth; right lower front incisor out.

Section—Cervical lymph glands enlarged and blood effused into them.

Brain lacerated; skull crushed in.

Medulla oblongata, under surface very vascular.

Larynx somewhat red; membrane of ventricle protrudes.

Œsophagus pinkish.

Stomach contains particles of hair, straw, grape skins, feathers.

Heart, blood coagulated.

Lungs ooze a sanious serum.

Liver congested.

Spleen, reddish, firm, weight $19\frac{2}{5}$ grams; length 16 cm., width at wider end 4 cm.; at other end, 1 cm.; thickness 5 mm.

Cultures from medulla oblongata, spleen, lymph glands and parotid, grown in gelatin; culture from lymph gland (cervical) in bouillon, placed in thermostat.

September 24th, 4 p. m., gelatin liquefied contaminatively (which the organism about to be referred to does not do).

Cultures in bouillon are very fetid, and exhibit lance-shaped cocci (bacilli); also bacilli with clear interspace and bipolar staining and curved chains of five or six; there is also a short, thick bacillus in gas vacuole; this organism is present in common putrefaction. The cultures from gelatin are less gross than those from bouillon, exhibit more clearly the intermediate clear space. The odor of gelatin cultures is as fetid as the bouillon; the above applies to cultures of the cervical lymph glands of dog 17 and the heart blood of rabbit R in gelatin, below referred to (rabbit R trephined from medulla of dog 17).

This bacillus with rounded ends, bipolar staining and clear interspace, varies in size in the same media, differs in size in different organs and structures; it is the well-known bacillus of rabbit septicæmia, and further reference to its morphology and mode of growth is out of place on this occasion; lenses of good definition are indispensable because the organism is often very short, and the clear interspace very narrow; easily mistaken for juxtaposed cocci.

The ordinary carbol-fuchsin stain, if allowed to remain but a few seconds on the cover smear, gives satisfactory results.

The following are the details of the experiment. On September 22d, 1893, three rabbits were trephined and 1 cmm. of the medulla oblongata of this dog, rubbed up in bouillon, was introduced beneath the dura. On this same occasion three rabbits were injected in the lumbar region hypodermically with 1 cc. of a bouillon mixture of medulla oblongata of this same dog; these rabbits were designated by letters; R, W and X were the three rabbits trephined.

Rabbit R died on the third day, rabbit W on the second day, and rabbit X on the second day.

The rabbits injected directly with the mixture of medulla oblongata in bouillon are indicated by the letters K, T, W.

Rabbit K died on the second day; T on the fourth day, and W on the second day.

Cultures made from the heart blood of all of these animals exhibited the organism described above.

Cultures from the heart blood of rabbit R, which was trephined from the medulla of dog 17, injected into rabbit Y, killed it in one day. This ends the trephining experiment.

Cultures from the heart blood of rabbits K and T (which rabbits were directly injected with

the medulla oblongata of the dog) killed rabbit Y′ in one day.

This ends the experiment with the medulla.

Referring to the post-mortem examination of dog 17, it will be seen that his cervical lymph glands were enlarged and blood effused into them. Cultures from the glands give the following interesting results: 1 cc. of the bouillon culture injected into rabbit Z killed it on the second day; this is the first remove from the dog.

Cultures of the heart blood of rabbit Z in Dunham's fluid were injected into rabbit Z′; it died on the second day.

Rabbit T′ was identically injected and also died on the second day; these rabbits are second removes from the dog.

Guinea-pig H, injected with 1 cc. culture of heart blood of rabbit Z in Dunham's fluid, died on the sixth day.

Guinea-pig G, injected with 1 cc. culture of heart blood of rabbit Z in gelatin, died on the sixth day. These guinea-pigs are second removes from the dog.

Mouse A, injected with 5 minims of culture of heart blood of rabbit Z in Dunham's fluid, died on the third day. This mouse is the second re-

move from the dog. Cultures from heart blood of this mouse A in Dunham's fluid injected into rabbits S′ and L′ killed them on the third day; this is the third remove from the dog. Cultures from heart blood of guinea-pig G (above mentioned) in Dunham's fluid injected into rabbits R′ and Q′ killed them on the second day; this is the third remove from the dog.

Cultures from the heart blood of this same guinea-pig G injected into pigeon A killed it on the seventh day; this is the third remove from the dog.

Rabbit N′ was injected with the culture of heart blood of pigeon A and died on the second day; this is the fourth remove from the dog.

The experiment ceased with the fourth remove from the dog.

Another, pigeon B, was killed by an injection of the culture of heart blood, this being also the fourth remove from the dog through mouse A.

All of these animals, as well as the cultures, exhibited the organism as described above.

Two white rats, three times injected, remain immune. It is to be noted that when other animals than rabbits have been killed by cultures, other rabbits have been killed by cultures from

these animals, constituting a return control experiment.

The signs and symptoms of this disease, septicæmia in the rabbit, ante-mortem and post-mortem, are markedly characteristic. The ante-mortem signs are somnolency and dyspnœa. The animal sits with its ears backward upon its body, its flanks panting laboriously, its eyelids constantly closing.

The alvine evacuations are pultaceous.

The temperature may rise to 106° F., which is one or two degrees above the normal maximum; this rise is very transient, rapidly falling, below the normal, three degrees; the minimum normal temperature in the rabbit being about 100° F.

Usually the animals die quietly, exceptionally convulsed. A constant post-mortem characteristic is the pale, salmon-colored, bloodless (anæmic), collapsed lung. The spleen is sometimes enlarged; the liver friable; the intestine has exhibited no lesion except perhaps increased vascularity.

The site of the injection usually shows increased vascularity, exceptionally sloughing.

Special attention must be directed to the

dyspnœa, which is hæmic, not pulmonary. The lungs are pallid and bloodless, or, more correctly stated, the blood is not red blood, the red blood corpuscles are not red; even when closely agminated, the color is only a faint yellow, and the single corpuscle has no color at all. Morphologically the red corpuscles are distorted, fail to maintain their sphericity, and many, like a globule of mercury, drag a tail; in addition to this poikilocytosis, there is a pseudo-nucleation caused by peripheral absence of protoplasm (hæmoglobin). This excessive liability to vacuolation of the corpuscles is general and takes place in different parts of the area of the cell. Sometimes the cell is emptied of its contents, the periphery alone as a mere ring remaining; sometimes as just noted, a zone between the circumference and the centre is vacuolated, leaving the centre as a seeming nucleus; the term excessive liability has been used advisedly, because cell vacuolation occurs as a post-mortem change; and as the result of reagents, especially acid stains (dyes); but this disintegration, this granular necrosis, this proneness of protoplasm to drop out, is an intra-vitam result of this organism, a pernicious anæmia.

Of great interest is the fact that this organism of rabbit septicæmia was obtained from the medulla of the dog, and it is not improbable that in certain diseases of the dog in which these animals act peculiarly and are regarded as rabid, they may be suffering from the effects of this organism.

What effect the organism of rabbit septicæmia would have upon the human animal has not been ascertained.

Sternberg[1] found the organism in the liver of a yellow fever corpse, though this liver had been wrapped up antiseptically. I have found this organism in a liver with small abscesses, cultures from which speedily killed mice and rabbits, and the cadavers quickly decomposed.

Ernst,[2] of Harvard, calls attention to the fact that in experimenting with rabies rabbits are apt to die of cords in a condition of early putrefaction. Whether this bacillus of rabbit septicæmia is an organism causing early putrefaction, and has its habitat ex corpore, or like the bacillus capsulatus lanceolatus, exists normally within the

[1] Sternberg, Manual of Bacteriology, 1892, p. 409.

[2] Ernst, American Journal Medical Sciences, April, 1887, p. 321.

body and only asserts its influence under certain conditions, is still unknown.

Davaine has shown that this organism is present in putrefying ox blood, but it is not passively present; it actively causes, is the agent of, decomposition; effecting not only post-mortem but ante-mortem destruction of the protoplasm, vitiation, ruination, of the hæmoglobin.

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RABIES IN THE MOUSE,

TOGETHER WITH A SIMPLIFIED EXPERIMENTAL METHOD FOR THE DETECTION OF RABIES.

It is often necessary to determine whether an animal has had rabies. It is especially important to decide this question when a suspected animal has bitten others or human beings. It is not proposed that any one should await the result of the experiment before resorting to treatment. But the demonstration has a scientific value in the compilation of statistics; moreover, if it prove the disease to be rabies, the wisdom of submitting to treatment is substantiated. If it is not, then there is no further source of anxiety. The method usually employed to determine this question is to trephine rabbits and inject some of the medulla of the suspected animal beneath the dura. This operation, though requiring but little skill, necessitates a number of instruments and appliances which the practitioner may not have; and rabbits are not always obtainable; when these animals are simply injected hypodermically the result is too frequently negative.

These objections do not apply to the house mouse. It is very susceptible to the disease, exhibiting the signs markedly, the disorder and impairment of motility being very evident when this active little animal is so situated as to enable it to exercise freely. A small cage with a compartment opening into a light tin and wire bar wheel, so constructed as easily to revolve, affords it opportunity to display its agility. It delights in turning the wheel, which it does rapidly and with exact coördination, never missing to place the foot upon the bar. The onset of rabies is shown in the slower movement, in missing the bar, in thrusting the extremity between the bars, and stopping often to rest. From this condition the disease develops in the direction of quiet or of excited rabies. In the former the mouse tends to rest. If undisturbed, the disease is not evident, there being only a degree of tremor; but, forced to move, the usual incoördination becomes manifest. It attempts to revolve the wheel, frequently missing the bar. At a further stage it turns the wheel with its fore limbs, the hind ones extended motionless and dragged behind paralyzed. In the excited form there is a tendency to restlessness; slight disturbance

causes it to stagger from one compartment to the other. It struggles to revolve the wheel, falling from side to side and over and over. Recovery even in this advanced stage is not impossible in the mouse. In the rabbit it has not been observed to occur when the symptoms have fully declared themselves.

So characteristic are the signs of this disease in the mouse that, except for the purpose of exhaustive demonstration, the transfer from mouse to rabbit is supererogative. It is readily transferable, as the cases cited in the table show.

The mice were injected in the subcutaneous tissue at the root of the tail. A piece from the floor of the fourth ventricle of the medulla—two cubic millimetres—was rubbed up in one cubic centimetre of bouillon. Of this five minims were injected with an ordinary hypodermic syringe.

In the return control experiments the medulla oblongata of the mouse was used to inject the trephined rabbits subdurally.

The source of the material in all cases except three was the medulla oblongata of rabid rabbits. These three exceptions which did not develop rabies were injected—one from the medulla ob-

longata of a rabid hen, one from the medulla of a rabid mouse, and one from a culture of medulla of a rabid man. Avian rabies is prob-

Tabulation in Detail.

No. of mouse.	Date injected.	First symptom noted.	Died of rabies.	Recovered.	Remarks.
1	Feb. 17.	Not noted.	9th day.	.....	Rabbits 117 and 118 trephined and affected with rabies.
2	Mar. 14.	8th day.	10th day.	.....	Rabbits 138, 139, and 140 trephined and affected with rabies.
3	Mar. 20.	7th day.	.....	Recovered.	
4	Mar. 20.	7th day.	.....	.....	Convalesced and relapsed; killed by accident March 30th; trephined rabbits 92 and 93, which became affected with rabies.
5	Apr. 3.	.....	.....	.....	Escaped.
6	Mar. 24.	11th day.	12th day.	.....	Rabbits 147 and 80 trephined and had rabies.
7	Mar. 24.	13th day.	14th day.		
8	Mar. 24.	.....	.....	.....	Died April 8th, accidentally.
9	Mar. 24.	.....	.....	.....	Escaped.
10	Mar. 24.	.....	.....	.....	Died April 1st, accidentally; trephined rabbits 101, 102, and 103 did not contract rabies.
11	Mar. 24.	11th day.	14th day.		
12	Mar. 24.	.....	.....	.....	Died March 26th, accidentally.
13	Mar. 26.	.....	.....	.....	Died March 28th, accidentally.
14	Mar. 29.	.....	.....	.....	Injected with medulla of hen; still living.
15	Mar. 30.	.....	.....	.....	Escaped; injected from medulla of mouse 4.
16	Apr. 2.	14th day.	17th day.	.....	Trephined rabbits 132 and 125.
17	Apr. 2.	.....	.....	.....	April 3d died; accidental death.
18	Apr. 2.	8th day.	9th day.		
19	Apr. 3.	6th day.	7th day.		
20	Apr. 9.	11th day.	14th day.		
21	Apr. 16.	8th day.	10th day.		
22	Apr. 16.	9th day.	11th day.		
23	Apr. 23.	.....	.....	.....	Escaped.
24	Apr. 28.	.....	.....	.....	Injected with culture of man's medulla; still living.
25	Apr. 28.	.....	.....	.....	April 29th, accidental death.
26	Apr. 30.	11th day.	12th day.		
27	Apr. 30.	11th day.	23d day.		
28	May 6.	14th day.	17th day.		
29	May 6.	8th day.	10th day.		
30	May 6.	11th day.	12th day.		
31	May 6.	9th day.	11th day.		

ably not transmissible to mammals, and cultures producing rabies are unknown; so that two of these cases must be classed with accidental deaths.

The total number of mice was 31.

Accidental deaths	8
Regular rabies	17
Recovered	1
Convalesced and relapsed	1
Escaped the disease	4

Subtracting from the total accidental deaths reduces the number to 23, 19 of which took rabies. If this is a maintainable average, then 82 per cent. of mice take the disease when hypodermically injected.

As a control to these experiments seventeen rabbits were trephined from the medulla of the mice and all died of rabies. Of these, several are noteworthy.

Rabbit 147 was trephined and injected subdurally from the medulla of mouse 6 (which had been injected at the root of the tail hypodermically with the medulla of rabbit 121), and developed rabies on the ninth day.*

* The material used was the thirteenth remove from the dog through the medulla oblongata of a horse which the dog had bitten. The virus at this remove had diminished the period of incubation from 15 to 9 days.

Rabbit 140, injected subdurally from mouse 2, developed rabies on the ninth day.

Rabbit 118, trephined from the medulla of mouse 1, had advanced rabies on the eleventh day; mouse 2, injected hypodermically from the medulla of this rabbit, developed rabies on the eighth day.

Rabbit 117, injected subdurally from the medulla oblongata of mouse 1, had advanced rabies on the eleventh day.

In conclusion, I may reiterate that in the mouse we have an animal which is easily experimented upon and in which the results are very pronounced and unmistakable. I therefore recommend highly the use of the mouse for the experimental determination of rabies.

RABIES.

A REPORT OF THE AUTOPSIES ON FOUR RECENT CASES OF RABIES AND A BACTERIOLOGICAL EXAMINATION OF THE RABID DOG, TOGETHER WITH THE RECENT LABORATORY EXPERIMENTS.

Four little human animals—the word is used advisedly not alone as expressing their social status, but in order to bring them within the pale of sympathy of the Society for the Protection of Animals. The horse that falls on the icy pavement comes within the pale of their work, and we should not forget that "men, too, have fallen with the harness on in wintry roads." Not in the heat of discussion, but after calm reflection, this assertion is made; that in conflict with the rights of human animals the lower animals have no rights. To save one fellow being, however lowly, I would sacrifice the entire breed of dogs, however high.

That there is such a disease as rabies this community has received most convincing evidence. The veterinary branch of medicine is

not skeptical on this subject, and in fact only a very few of those who have never seen the disease deny its existence. The highest proof that one can ask is demonstration, and rabies is an exquisitively demonstrable disease. But, convince a man "against his will and he is of his own opinion still," applies to the man whose sympathies and brains have gone to the dogs.

It is the consensus of medical opinion that the dogs that run at large are the ones that contract rabies. The disease is the result of the application of the virus of rabies. Seclude a dog and he cannot take the disease. It has not been so long since a man brought me a Skye terrier, which he said had been lying quietly by the stove and, suddenly rushing over, bit him, his wife and child. I found the stomach containing food, and I asked him if the dog had been out. He answered, "No, it is always kept in the house." I said, "You need have no fear, you cannot take rabies from this bite." With regard to the dogs of Constantinople, it was formerly said that they never took rabies, but finding that they did, these statements were modified to say that they seldom took it. Of course, it only takes place when a mad dog runs amuck in the neighborhood.

Now I do not know anything about canine rabies, but I can talk about it. For the constitution of the United States guarantees freedom of speech, though it cannot qualify a man to reason upon a subject about which he is ignorant. There is, however, compensation in many things, and while the constitution allows everybody to speak, it compels nobody to answer; and we have another very high authority which says, "It is written answer, and again it is written answer not." Life would not be worth having if one were compelled to answer every hypothesis that some brains originate on the slightest occasion of excitement.

There are two forms of canine rabies: in one the dog is first maniacal and then becomes paralyzed, and in the other form he is paralyzed from the first. The dog with rabies is sometimes exceedingly affectionate, but this condition may last but a short time before it develops into the maniacal form. Of course, the saliva is as virulent in one form as in the other.

With regard to the dog in question, it was a large one and seemed to be a cross between a Newfoundland and a mastiff. On post-mortem there were the usual negative appearances; con-

gestion of the kidneys and lungs, and possibly of the bladder. One thing that led me to believe it was rabies was the inflamed condition of the lymphatic glands. The stomach contained pieces of glass, hair and straw. A dog may have all these appearances and not have rabies, but, taking the whole thing into consideration, the peculiar behavior of the dog, etc., it would be best in such a case to give the people the benefit of the doubt and call it rabies. I saw only three of the boys bitten by this dog; four of the eight died. In addition to these three I had seen another case a few years ago.

The public idea is that the disease prevails in dog-days, but in general it is more common in the spring and fall than in the summer. Three years ago Dr. Sappington asked me to see a case in the same neighborhood as these last cases. The little fellow was semi-recumbent on the couch and complained that opening the doors annoyed him, and the air hurt his head and face. He had been delirious but spoke with clearness.

He would have a clonic convulsion during which he seemed to be struggling with some one, but he was conscious all the way through. If you sat opposite him he talked to you until the

convulsion came on, when his attention was altogether distracted. His pupils were dilated and the anterior chamber rather deep. He had another symptom that was almost pathognomonic, that is, sputation. He would spit saliva in little pools on the carpet and apologize to his mother for soiling the room. When these convulsions passed off he would get up, put on his clothing, walk to the window, and then would come back to the couch and have another convulsion. It was about 11 o'clock that I saw him, and he died that night. He would not have impressed anyone at the time as being so ill as to die in such a short time.

The cases that are at present attracting attention: The little boy Henry was bitten on the first of December, had gone to New York before the end of that week, returned on the 18th, and was sick on his way home. I saw him a day or two afterward through the kindness of Dr. Mitchell and Dr. Pillsbury, and there was almost the same condition of things that I have just related; delirious one instant, rational the next. He first thought we had come to kill him, and believed that all the boys bitten must be killed. His physician asked him to drink a po-

tion containing some bromide of potash and chloral. He looked at it, carried it to his mouth, and with a desperate struggle did manage to get some little down. This was about 11 o'clock at night. I went to see him again at 5 o'clock the next evening, but he died just before I reached there.

The next case is one in which rabies manifested itself in a different way. This has sometimes made the ground for questioning the disease. You are told that it is not the same in the rabbit and dog as in the human animal. Rabies in the rabbit is typical of paralytic rabies. This case is one of that kind. The boy, Eppers, had gone to New York early, perhaps on the third, and returned about the eighteenth of the month. When I saw him he had ptosis of the left eyelid, and could not shut his mouth. For this reason he could not expectorate, but he had a handkerchief with which he continually wiped away the excessive secretion from his mouth. He talked altogether with his larynx. When attempting to walk his feet would swing passively about in an incoördinate way. When asked to drink he simply refused and said he would not try. He died the same night.

The third boy I saw when there was nothing to be told. There was nothing in his case of particular interest. The points of interest are the evidence we possess that the dog was rabid and the evidence just given, which may be called clinical evidence.

Upon this paper (exhibiting paper) there is a synopsis of experiments showing that the dog was rabid. A piece of the dog's medulla was made into an emulsion with water. With this three trephined rabbits, A, B, C, were inoculated. The first developed rabies on the fifteenth day and died the same day; B on the nineteenth day and died on the twentieth; C on the seventeenth day, but I killed this rabbit the same day and with its cord inoculated three other rabbits. To complete this experimental evidence it took twenty-two rabbits, and the work extended over two months. From this rabbit that I killed, one of the three others injected died accidentally on the fourth day, a second developed rabies on the nineteenth day and died on the twenty-second, and the third developed it on the twenty-first and died on the twenty-third day. This is adequate proof to demonstrate that the dog had rabies. The reason for using the second series

of rabbits was this: It is claimed that sometimes there is a descending neuritis that causes similar symptoms and conditions to rabies, so this number lessens the possibility of such things.

Here (showing papers) are experiments to demonstrate that the Henry boy died of rabies; rabbits trephined from that boy. I trephined the rabbits on the evening of his death. Rabbit A developed rabies on the sixteenth day and died on the eighteenth, B on the fourteenth day and died on the eighteenth, C on the seventeenth and died on the eighteenth, and D on the eighteenth and died on the twentieth day. From rabbit A I trephined two rabbits, K and W. K developed the disease on the fourteenth and W on the fifteenth day; they both died on the eighteenth, which goes to prove that they did not die of the laboratory virus. That virus is probably 300 or 400 removes. The virus with which these children were treated would have developed rabies, if that gave it to them, on the seventh day, and they would probably have been dead on the twelfth day. These experiments are sufficient to prove that the dog was mad, that the boys died of rabies, and that the virus was that of the dog and not that of the laboratory.

I believe it is scarcely necessary to confirm these demonstrations of the same kind that I made from the boy Eppers. The same experiments were made upon two sets of rabbits and none developed disease earlier than the fourteenth day. I think it is sufficiently proven that the virus was not the laboratory virus and not the result of the treatment. But the community has naturally come to doubt the efficacy of the treatment, and, if they do not positively impugn it, they say it had no effect, and that it was useless. To prove its utility one must get at its statistics, and to have them of value must eliminate all sources of error. There are three columns, one of which contains the cases in which the dog is demonstrated to have been mad. That column is a good one and is sustained. The next is that in which the dog is asserted to have been mad upon the certificate of a veterinarian and is probably accurate, but in the third the evidence is based on suspicion. This embraces the cases in which the animal has disappeared. (See p. 348.)

Two of these boys were bitten on the cheek, one upon the back of the neck, and the fourth

over the eye. Now it is estimated that of bites upon the face, without treatment, 82 per cent. will prove fatal, and with treatment 80 per cent. are curable.

SCHOOL OF MEDICINE
UNIVERSITY OF LEEDS

THE TECHNIQUE OF THE PASTEUR ANTI-RABIC TREATMENT.

When a person has been bitten by an animal that may have been rabid it is very important that this should be ascertained. The signs and symptoms, ante- and post-mortem, afford evidence of the nature of cumulative probability, approximating certainty, which can be absolutely demonstrated only by animal experimentation.

If a rabbit or guinea-pig be trephined and a few drops of an emulsion from a small piece of the medulla oblongata of the suspected animal be injected beneath the dura, rabies, if present, discloses itself in about 15 days with invariable uniformity in semiology. The first sign being tremor, a side-to-side shaking, when disturbed; soon the animal staggers and falls when running; this incoördination eventuates in paralysis; convulsions may also occur. Death takes place some time during a period of about 72 hours. If from the medulla oblongata of the first rabbit a second be trephined, from this the third, and so on until about a series of 50 have been so treated,

the period of incubation lessens from 15 to 7 days, the cords of the latter constitute a fixed virus, and are used in the prophylactic treatment of the disease by hypodermic injection.

The course of the disease from inoculation to death is about 12 days, so that a few over 30 are all the transmissions that can be effected in a year. The Paris virus at this institution is 472 passages (beginning with the medulla oblongata of a rabid cow) through the rabbit.

I have the one hundred and nineteenth passage through the rabbit, which was started by trephining and injecting the medulla oblongata of a rabid cow. I was occupied about four years in accomplishing this. From the medulla oblongata of a rabid horse I also passed the virus from rabbit to rabbit until the tenth remove was reached.

Being curious to ascertain the susceptibility of the mouse to this disease, this little animal was injected hypodermically at the root of the tail with a few drops of an emulsion in sterilized water from the medulla oblongata of the tenth remove rabbit through this horse above referred to. The mice were then placed in cages with revolving wheels, which they delight in turning,

and this they do with great dexterity, never missing in placing their feet upon the bars. The first sign of the disease is a disturbance of this precise coördination. It frequently misses the bars, thrusting its legs between them, and finally becoming so paralyzed that it turns the wheel with its fore limbs, the hind ones, stiffly and motionlessly, extended backwards. Take a piece of the medulla oblongata of one of these mice when dead and trephine a rabbit, injecting a few drops of emulsion as before. This rabbit, after the proper incubation, reproduces the disease with the same signs and symptoms. If this disease does not fulfil the requirements of specificity no disease does.

This virus of rabies, so persistent under favorable conditions, is easily destroyed. Below 68° F. and above 78° F. it deteriorates and is destroyed rapidly at 118° F. This is exemplified in the gallinaceous fowl. A hen has a normal temperature of about 108° F.; when trephined and an injection of rabic virus made subdurally, it does not develop the disease until a lengthy period of incubation, 20 to 30 days or more. The fowl, though completely paralyzed, may recover. Should it die the disease cannot be com-

municated to rabbits by trephining and subdural injection of the medulla oblongata of the hen dead after this long course of disease. The virus has been rendered inert, probably by lengthy exposure to the normal high temperature. If, however, the hen be killed 15 days after trephining its medulla oblongata will be found virulent and will convey the disease.

The technique for the determination of rabies is simple and the result certain unless the cord has undergone putrefaction, when it will kill the rabbits in about 48 hours with sepsis. Should they escape this or recover from it they will die of rabies. Putrefaction does not necessarily destroy the virus. The operation of trephining is painless and requires no anæsthetic, the use of which I have long abandoned, and it is no longer used at the Institut Pasteur in Paris.

EXPERIMENTAL RABIES,

WITH ESPECIAL REFERENCE TO THE BALTIMORE CITY CASES.

Rabies is a specific contagious neurosis, affecting markedly and peculiarly the nervous system, and capable of unlimited propagation by inoculation. The only certain proof of the existence of this disease is experimental demonstration. Preferably the inoculated material is a portion of the floor of the fourth ventricle (medulla oblongata), which is introduced subdurally by trephining rabbits. By this method the Institut Pasteur, Paris, starting with the medulla oblongata of a cow that had rabies from the bite of a rabid dog, has passed the disease from rabbit to rabbit until the four hundred and eightieth remove has been reached. Two rabbits having been trephined each time, this gives 960 rabbits which have taken the disease.

On October 5th, 1893, I received from William R. Tatum, D. V. S., Brighton, Md., the medulla oblongata of a cow that had rabies from the bite of a rabid dog. Starting with this me-

dulla and trephining from rabbit to rabbit, the one hundred and twenty-eighth remove has now (August, 1897) been reached. Seven hundred and thirty-one rabbits have in this way been given rabies. Using the medulla oblongata of a rabid horse, I have passed the disease from rabbit to rabbit to the tenth remove; 60 rabbits were the subjects of this experiment. Three times from the medulla oblongata of the human being I have produced the disease in rabbits. One was from a colored man who sustained a not severe bite—a slight wound over the left eye. The man was attended by Dr. William E. Magruder, of Olney, Md. His medulla oblongata was received from Dr. Tatum. Two rabbits trephined and subdurally inoculated April 19th, 1894, developed rabies May 3d, 1894, and died May 6th, 1894. The two other victims were children, boys, aged eight years and 15 years. They are two of the four persons who died out of eight bitten by the same dog. These cases have been designated as the Baltimore cases of rabies. On December 1st, 1896, a large dog, cross between St. Bernard and mastiff, bit eight boys in Baltimore City Annex. Of these boys four died of rabies within 36 days after having

been bitten, and within 19 days after the termination of treatment by the Pasteur method in New York. The bites were severe in character and situated on the bare face and neck.

1. Wilson, aged 11 years. Seat of bite on face over left eye. Not cauterized. Date of discharge, December 17th, 1896. Date of bite, December 1st, 1896. Date of first treatment, 42 hours after bite. Date of death, January 5th, 1897, 18 days after treatment.

2. Perry, aged 16 years. Seat of bite on cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, 77 hours after bite. Date of death, December 26th, 1896, eight days after treatment.

3. Eppers, aged 15 years. Seat of bite, back of neck. No efficient cauterization. Date of discharge, December 17th, 1896. Date of first treatment, 50 hours after bite. Date of death, December 26th, 1896, nine days after treatment.

4. Henry, aged eight years. Seat of bite, left cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, 77 hours after bite. Date of death, December 21st, 1896, three days after treatment.

A boy named Kiel was bitten on the ear, but through an ear warmer, and therefore must be excepted from the class of bites on bare parts. All bitten on the bare face and neck died; all the others escaped. They are:

5. Perry, aged 18 years, brother of No. 2, bitten on the arm.

6. Ashley, aged ten years, bitten on arm.

7. Buhl, aged 14 years, bitten on arm.

8. Kiel, Joseph, aged 15 years, bitten on ear through an ear warmer.

The foregoing is a necessary preliminary statement. The chief object of this communication is to bring before the medical profession the experimental details proving that the dog had rabies, and that two of the boys, Henry and Eppers, also had it. In the other two cases a post-mortem examination was not obtainable. Also that the virus was from the dog and not from the treatment.

The following is the post-mortem examination of the dog, December 2d, 1896, 2 p. m.: Cross between St. Bernard and mastiff; yellow, with white neck; weight, over 100 pounds; shot after having bitten eight boys, chickens, and dogs. Hard palate, dark bluish in color. Rigor mortis

marked. Brain soft. Medulla oblongata soft, and softening around central canal of spinal cord. Lungs ooze freely bloody froth. Kidneys, dark red cortex. Bladder empty. Liver normal. Spleen normal. Stomach contains pieces of wood and stone, straw, horsehair—mane or tail. Larynx, blood in, from wounds in mouth. Trachea, blood in, from wounds in mouth. Heart normal. Lymph glands, cervical, blood effused into.

December 2d, 1896, 2 p. m.: Trephined three rabbits and injected beneath the dura 3 minims of an emulsion of the medulla oblongata of this dog in sterilized water.

	Rabbit A.	Rabbit B.	Rabbit C.
December 8th.....	T. 103.5°F.	T. 103.8°F.	T. 103.4°F.
December 11th.....	103.7	103.9	103.8
December 14th.....	102.5	102.5	102.5
December 15th.....	103	103	104.4 (Cried out when held.)
December 16th, 2 p. m.	102.2 (Vigorous, no disorder of motility.)	103	104.3
5.20 p. m.....	102.2	103	104.8
December 17th, 15th day, 2 p. m....	105.1 (Cries out and incoördinate; died 5 p. m.; observed to be sick 7 a. m.)	102.7 (Very active, runs about.)	103.2 (Ears erect; legs outstretched; very incoördinate.)
December 18th, 2.30 p. m.....		102.8	99.2
December 19th, 17th day.....		103.2 (Dull but runs when incited.)	(C killed; trephined 3 rabbits, D, E, F.)
December 20th, 18th day.....		99.8 (Very incoördinate, runs about, falling over and over; died this night.)	

December 19th, 1896: Killed rabbit C on seventeenth day after inoculation. Trephined and injected the emulsion of its medulla oblongata in sterilized water subdurally into rabbits D, E, and F. Amount injected, 5 minims.

	Rabbit D.	Rabbit E.	Rabbit F.
December 22d.....	(Died accidentally.)		
December 29th.....		T. 103.5°F.	T. 103.8°F.
December 30th.....		103	102.3
December 31st.....		103.5	102
January 1st, 1897.....		104	103
January 2d		104	102
January 3d, 15th day		103	102
January 4th.....		102.2	101.6 (Dull, sluggish.)
January 5th.....		102.7	103.3 (More alert.)
January 6th.....		104	100.7 (Dull, stiff in movement.)
January 7th, 19th day.....		101.3 (Gritting teeth.)	97.8
January 8th.....		100.3 (Runs around but slips sideways.)	97.5 (Helpless on side.)
January 9th.....		97 (Runs around but very incoördinate; gritting of teeth marked.)	(Found dead on 21st day.)
January 10th.....		94.2 (Helpless on side; grits teeth; slight convulsions.)	
January 11th.....	(Found dead 23d day.)		

Thus five rabbits have been given rabies from this dog; three immediately from the dog, two from one of these rabbits, this rabbit having been killed in order to stamp a suggestion of putrefaction as a fallacy. The latter experiment

proves the disease to be an infectious neurosis, not a traumatic degeneration.

Experiment demonstrating that Robert Henry, aged eight years, of Baltimore, died of rabies. He underwent Pasteur treatment in New York, arriving there about December 4th, 1896, and returning to Baltimore on the night of December 18th, 1896, being then sick. He died of rabies, December 21st, 1896, 5 p. m. He had been bitten on December 1st, 1896. Post-mortem examination, December 21st, 1896, 7 p. m.

December 21st, 1896, 9.30 p. m.: Four rabbits were trephined and injected subdurally with emulsion in sterilized water of the medulla oblongata of the boy Henry. Amount injected, 5 minims.

	Rabbit G. Temp.	Rabbit H. Temp.	Rabbit I. Temp.	Rabbit J. Temp.
December 26th, 5th day	103.2°F.	104°F.	103.5°F.	103.8°F.
December 27th.....	103.8	103.8	104	104.8
December 28th.....	103.6	103.2	104.2	104
December 29th.....	103.5	104.1	104	103.9
December 30th.....	103	102.5	103	104.5
December 31st.....	103.5	101.5	102.6	106
January 1st, 1897.....	103.2	103.2	102.5	104.6
January 2d	102.5	103.3	103.5	102.5
January 3d	102.8	101.8	103.6	102
January 4th.....	101.5	100	103	102
January 5th, 15th day.	101	99	102	102.3
January 6th.....	97.8	96.6	102.6	102.2
January 7th, 17th day.	(Dead.)	97.4 (Died 2 p. m.)	(Found dead.)	
January 8th.....				95
January 9th, 19th day.....				(Found dead.)

H is dull, stiff, and tremulous, with wound torn open, on the fourteenth day after trephining.

G lies flat on side, hind legs outstretched, creeping, crouching movement, on fifteenth day.

I grits teeth, stiff in movement, incoördinate, on fifteenth day.

J very incoördinate, falling over and over, on sixteenth day.

Experiments demonstrating that the boy Henry died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit was a specific infection and not a traumatic degeneration (neuritis, ascending or descending).

January 7th, 1897, 2 p. m.: Rabbit K trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally inoculated from medulla oblongata of boy Henry on December 21st, 1896.

			Temp. of Room.	Temp. of Rabbit.
January 13th, 1897,	2 p. m.,	7th day..	55°F.	102°F.
January 14th,	1 p. m.,	8th day..	55	103.4
January 15th,	1 p. m.,	9th day..	60	102.1
January 16th,	1 p. m.,	10th day..	58	102

This rabbit is pregnant, paws at floor of cage,

is excited, and occasionally utters a subdued grunt. These actions are common to pregnant rabbits and may have no significance as regards rabies.

		Temp. of Room.	Temp. of Rabbit.
January 17th, 1897,	1 p. m., 11th day..	58°F.	101.7°F.
January 18th,	1 p. m., 12th day..	62	101.5
January 19th,	1 p. m., 13th day..	60	101.3
January 20th,	1 p. m., 14th day..	54	101.3

Rabbit when laid on floor cannot rise, unable to get up, but when held up by the integuments of the middle of the back it can kick and strike vigorously. This is paralytic incoördination.

		Temp. of Room.	Temp. of Rabbit.
January 21st, 1897,	1 p. m., 15th day..	66°F.	98.8°F.

Helpless on side with limbs outstretched.

		Temp. of Room.	Temp. of Rabbit.
January 22d, 1897,	1 p. m., 16th day..	66°F.	96.2°F.
January 23d,	1 p. m., 17th day..	57	94.5

Can still kick feebly when held up by back.

January 24th, 1897, 9.30 a. m., 18th day, found dead.

January 7th, 1897, 2 p. m.: Rabbit L trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896.

			Temp. of Room.	Temp. of Rabbit.
January 13th, 1897,	2 p. m.,	7th day..	55°F.	102.7°F.
January 14th,	1 p. m.,	8th day..	55	103.8
January 15th,	1 p. m.,	9th day..	60	103.9
January 16th,	1 p. m.,	10th day..	58	103.5
January 17th,	1 p. m.,	11th day..	58	102.5
January 18th,	1 p. m.,	12th day..	62	102.5
January 19th,	1 p. m.,	13th day..	60	102.6
January 20th,	1 p. m.,	14th day..	54	101.7

No coarse manifestation, but the temperature drop is significant.

			Temp. of Room.	Temp. of Rabbit.
January 21st, 1897,	1 p. m.,	15th day..	66°F.	100°F.

The rabbit assumes a crouched position. It is unable to sustain its body erect on pelvis and scapula. Motility of limbs impaired, hind legs almost completely paralyzed. Falls over on its sides at intervals. This crouched attitude (paralytic rabies) has been a characteristic feature of the disease in most of these rabbits.

			Temp. of Room.	Temp. of Rabbit.
January 22d, 1897,	2 p. m.,	16th day..	66°F.	97°F.
January 23d,	1 p. m.,	17th day..	57	96

Much emaciated.

January 24th, 1897, 9.30 a. m., 18th day, found dead.

Experiment demonstrating that the cord of rabbit G was not virulent on the ninth day, and therefore the virus with which G was inoculated subdurally was from the dog and not from the treatment.

January 7th, 1897, 2 p. m.: Rabbit M trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896.

	Temp. of Room.	Temp. of Rabbit.
January 13th, 1897, 2 p. m., 7th day...	55°F.	101°F.

Somewhat off food; transferred to warm box.

	Temp. of Room.	Temp. of Rabbit.
January 14th, 1897, 1 p. m., 8th day...	55°F.	102°F.

Rabbit is very unwell, very thin. Sweats about muzzle. Breath fetid like gangrene. This is an intercurrent malady and has no connection whatever with rabies or with the experimental inoculation. This disease occurs not infrequently among rabbits that have been subjected to no experiment. There is reason to regard this disease as contagious, infectious. It has as a symptom diarrhœa. There is no disturbance of motility.

January 15th, 1897, 9th day, found dead.

Two rabbits, O and P, trephined from this rabbit, developed no disease whatever. They were under observation for three months. This

proves that this disease cannot be communicated by subdural injection of the medulla oblongata; also that the medulla oblongata did not contain the virus of rabies on the ninth day, which it would have contained had the virus been that of the treatment.

Rabbit N was subjected to the same experiments as rabbit M, and died of the same disease on the eleventh day after trephining. It is to be regretted that no experiment was made to ascertain the condition of the medulla oblongata at this date, as regards the virus of rabies.

Rabbits M and N were in the same box all the time.

Experiments demonstrating that Conrad Eppers, aged 15 years, Baltimore, died of rabies. He underwent Pasteur treatment in New York, arriving there about December 2d, 1896, and returning to Baltimore December 17th, 1896. He died of rabies December 26th, 1896, 12.05 a. m. He had been bitten on December 1st, 1896. Post-mortem examination December 26th, 1896, 11 a. m.

December 26th, 1896, 6 p. m.: Four rabbits were trephined and injected subdurally with emulsion in sterilized water of medulla ob-

longata of the boy Eppers. Amount injected, 5 minims. Rabbits designated by letters Q, R, S, T.

RABBIT Q.

January 5th, 1897, 11th day, temperature..... 103.3°F.
January 8th, 14th day, temperature..... 103.3
January 9th, 15th day, temperature..... 102.7
January 10th, 16th day, temperature..... 103.2

Does not eat. Occasional gritting of teeth at long intervals. Ears at times erect. Runs about actively. In warm pen.

January 11th, 1897, 17th day, temperature..... 97.4°F.

Excited and very incoördinate.

January 12th, 1897, 7 a. m., 18th day, found dead.

RABBIT R.

January 8th, 1897, 14th day, temperature..... 98.4°F.
January 9th, 15th day, temperature..... 99
January 10th, 16th day, temperature..... 96

Marked paralytic rabies. Crouching, creeping, trembling, incoördinate movement. Had been in a cool box. Transferred to warm pen.

January 11th, 1897, 8.30 p. m., 17th day, temperature. 96°F.
January 12th, 7 a. m., 18th day, found dead.

RABBIT S.

January 8th, 1897, 14th day, temperature..... 103.2°F.
January 9th, 15th day, temperature..... 103

Marked paralytic rabies. Crouching, creeping movement.

January 10th, 1897, 16th day, temperature (in cool box) 98°F.
January 11th, 12 m., 17th day, found dead.

RABBIT T.

January 8th, 1897, 14th day, temperature..... 101.5°F.
January 9th, 15th day, temperature..... 101
January 10th, 16th day, temperature..... 99.9

Excited and incoördinate.

January 11th, 1897, 17th day, temperature..... 99.4°F.

Partly paralyzed. Jerking of head sideways.

January 12th, 1897, 18th day, temperature..... 97°F.

Aborted three fœtuses. Ears erect, legs sprawled out. Falls from side to side when it moves.

January 13th, 1897, 19th day, temperature..... 94°F.

Kicks and cries feebly.

January 14th, 1897, 1 p. m., 20th day, found dead.

Experiments demonstrating that the boy Eppers died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit is a specific infection and not a traumatic degeneration (ascending or descending neuritis).

Rabbit U trephined and subdurally injected with emulsion of medulla oblongata, that of

rabbit S, which died of rabies on the seventeenth day, January 11th, 1897, after having been trephined and subdurally injected from medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896.

January 7th, 1897: In attempting to get temperature (the thermometer was introduced per anum almost its entire length) the instrument was broken inside the bowel and considerable hemorrhage resulted.

		Temp. of Room.	Temp. of Rabbit.
January 18th, 1897,	1 p. m., 8th day..	62°F.	104.5°F.
January 19th,	1 p. m., 9th day..	60	102.3
January 20th,	1 p. m., 10th day..	54	102.2
January 21st,	1 p. m., 11th day..	66	101.5
January 22d,	2 p. m., 12th day..	66	101.4
January 23d,	1 p. m., 13th day..	57	98.5

Crouching, squeals, uses limbs with difficulty. Seemed dull and inactive on the twelfth day.

		Temp. of Room.	Temp. of Rabbit.
January 24th, 1897,	1 p. m., 14th day..	57°F.	97.4°F.

Helpless on side.

		Temp. of Room.	Temp. of Rabbit.
January 25th, 1897,	1 p. m., 15th day..	47°F.	94.3°F.

Feeble, convulsive movement.

January 26th, 1897, 12 m., died.

No inflammation within abdomen. No trace

of the broken-off thermometer bulb could be found. This accident happened in another case and does not seem to be productive of bad results.

Rabbit V trephined and subdurally injected with emulsion of medulla oblongata of rabbit S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896.

	Temp. of Room.	Temp. of Rabbit.
January 17th, 1897, 1 p. m., 7th day...	58°F.	105.3°F.

Rabbit has diarrhœa. It is doubtful if this rise of temperature can be attributed to incipient rabies, because it is too early.

	Temp. of Room.	Temp. of Rabbit.
January 18th, 1897, 1 p. m., 8th day..	62°F.	103.8°F.
January 19th, 1 p. m., 9th day..	60	103.2
January 20th, 1 p. m., 10th day..	54	102.2
January 21st, 1 p. m., 11th day..	66	104
January 22d, 1 p. m., 12th day..	66	105.4

This elevation of temperature may be attributed to incipient rabies, but the fact that on the seventh day a like rise occurred gives room for doubt.

		Temp. of Room.	Temp. of Rabbit.
January 23d, 1897,	1 p. m., 13th day..	57°F.	103.9°F.
January 24th,	1 p. m., 14th day..	57	102.3
January 25th,	1 p. m., 15th day..	47	101.7
January 26th,	5 p. m., 16th day..	47	102

Stiff in hind legs; sidelong movement.

		Temp. of Room.	Temp. of Rabbit.
January 27th, 1897,	1 p. m., 17th day..	47°F.	99.4°F.

Stiff, slow, sidelong movement.

		Temp. of Room.	Temp. of Rabbit.
January 28th, 1897,	1 p. m., 18th day..	47°F.	95.2°F.

Helpless on side.

January 29th, 1897, 9 a. m., 19th day, found dead.

Rabbit W trephined and subdurally injected with emulsion of medulla oblongata of rabbit S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected with medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896.

		Temp. of Room.	Temp. of Rabbit.
January 17th, 1897,	1 p. m., 7th day..	58°F.	103.9°F.
January 18th,	1 p. m., 8th day..	62	103.6
January 19th,	1 p. m., 9th day..	60	104
January 20th,	1 p. m., 10th day..	54	102.8
January 21st,	1 p. m., 11th day..	66	104
January 22d,	2 p. m., 12th day..	66	105

An up temperature, whether incidental or accidental.

		Temp. of Room.	Temp. of Rabbit.
January 23d, 1897,	1 p. m., 13th day..	57°F.	103.8°F.
January 24th,	1 p. m., 14th day..	57	101.7

Temperature drop. Exhibits no impairment of motility. Eats and seems well.

		Temp. of Room.	Temp. of Rabbit.
January 25th, 1897,	1 p. m., 15th day..	47°F.	101.5°F.
January 26th,	5 p. m., 16th day..	47	102
January 27th,	1 p. m., 17th day..	47	99.4

Decided temperature drop, but no motor disturbance. Still active, agile.

		Temp. of Room.	Temp. of Rabbit.
January 28th, 1897,	1 p. m., 18th day..	47°F.	98.6°F.

Very stiff and tremulous.

		Temp. of Room.	Temp. of Rabbit.
January 29th, 1897,	1 p. m., 19th day..	52°F.	94.5°F.

Stiff, tremulous, moves with difficulty, incoördinate.

January 30th, 1897, 1 p. m., 20th day, temperature too low for thermometer to register.
January 31st, 1897, 8 a. m., 21st day, found dead.

Rabbit X trephined and subdurally injected with emulsion of medulla oblongata of rabbit S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected with emulsion of medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896.

			Temp. of Room.	Temp. of Rabbit.
January 17th, 1897,	1 p. m.,	7th day..	58°F.	103.3°F.
January 18th,	1 p. m.,	8th day..	62	103.4
January 19th,	1 p. m.,	9th day..	60	103.4
January 20th,	1 p. m.,	10th day..	54	104.8
January 21st,	1 p. m.,	11th day..	66	104.8
January 22d,	2 p. m.,	12th day..	66	103.8
January 23d,	1 p. m.,	13th day..	57	103.7
January 24th,	1 p. m.,	14th day..	57	102.3
January 25th,	1 p. m.,	15th day..	47	102.3
January 26th,	5 p. m.,	16th day..	47	99.8

Decided temperature drop. Stiff and sprawled movement of hind legs. At one time marked incoördinate jerking.

			Temp. of Room.	Temp. of Rabbit.
January 27th, 1897,	1 p. m.,	17th day..	47°F.	96.4°F.
January 28th,	9 a. m.,	18th day, found dead.		

PRACTICAL NOTES RELATIVE TO RABIES.

At what time and under what circumstances should patients be advised to submit to treatment? With what material and in what manner are they treated? What risk attends treatment? If a human being contracts rabies, he inevitably dies. There are no verified cases of recovery. Three cases are recorded in which general paralysis developed during treatment. They all recovered. In one case, the treatment was not discontinued. Whether these were cases of paralytic rabies cured by treatment is a question regarding which a consensus of opinion has not been attained. Treatment should be resorted to as soon as possible. Delay is not only dangerous, but may be deadly. A physician consulted me regarding a bite upon his hand. He had already delayed ten days, awaiting the result of an inoculation experiment. He was advised to take treatment without further delay, but failed to do so. He developed rabies about as soon as the inoculated animals. Two patients were advised to submit

to treatment at once. They refused, stating they would await the result of the inoculation experiment. Rabies developed almost simultaneously in both the experiment and patients. However, a number, though not treated, escaped. An example of this was a child bitten severely on both arms. The dog had been experimentally demonstrated rabid.

As to risk, there is none greater than the rare and unjustifiable occurrence of abscesses. Lumps caused by proliferation of connective-tissue corpuscles are common, as is also a local or general erythema. The length of time of treatment should not be less than twenty-three days. If very severely bitten, and there is persistent induration about the wounds, it is advisable to continue treatment off and on until the induration subsides. Unless it is certain that rabies is absent, those exposed should not be held pending investigation. The affirmative result of the morbid histology, or experimental inoculation, is a demonstrated certainty. If there is a suspicion of rabies, the patient should be given the benefit of the doubt and should be treated without delay.

If the biting animal can be securely kept, it is a mistake to kill it. Treat the patient and ob-

serve the animal. If after a few days it is evidently in sound health, the treatment may be stopped. A lady seeking her stray dog visited a pound. She did not find her dog, but the good and amiable points of another dog were pointed out to her, to observe which she had to stoop over the animal, whereupon it seized and severely lacerated her lip with its teeth. This being a very dangerous situation for such wounds, she was treated at once and the dog visited for four days. It became evident that it was merely a vicious brute, and treatment was discontinued.

This question is frequently asked: What kind of serum is used in treatment? It is not serum. There is no serum antitoxin analogous to that of diphtheria. The therapeutic material used is a portion of the spinal cord of a rabbit that has died of rabies. This is rubbed up in sterile cool water. These spinal cords have been dried over caustic potash which diminishes the amount of virus, but does not attenuate it. The virus is in a condition termed fixed (*virus fixe*). This is a virus which, inoculated subdurally in a rabbit, causes rabies after six days. Before it attains this condition of fixation, it is necessary to inoculate from rabbit to rabbit until it has passed

through about fifty. In the first inoculation, rabies does not develop until the completion of eleven, twelve or fifteen days. The medulla oblongata is used in the inoculations of animals. Prior to experience it seems rash to inject a deadly virus into a human body. Pasteur demonstrated its harmless efficacy. The immense gulf between scientific audacity and foolhardiness had been securely bridged with experiments. The method of treatment is subcutaneous hypodermic injections. For convenience, the abdominal region is selected.

Among fanciful methods of treatment, there is the madstone. If it adheres virus is present; if it becomes coated with green, there is virus extracted; perhaps this really is the green pus organism. Raw livers of rabid dogs have been fed to patients. The brains of rabid rabbits have been suggested as therapeutic food.

In India the entrails of an insect are administered, which causes bloody purgation. The patient is also exposed to the heat of the sun. This remedy caused bloody dejections in an inoculated rabbit, but it in no way modified the fatal result.

Bile renders the rabic virus inert, but this mixture fails to confer immunity. The destruction of

virulence probably is due to cholic acid (M. H. Valée, of Toulouse, *Annales de l'Institut Pasteur,* June, 1899). Out of the body rabic virus is sterilized at a temperature of 108° F., which is the normal temperature of a hen. In this fowl, when subdurally inoculated, the disease runs a protracted course, and its medulla oblongata becomes inert, sterile. The temperature of a living, inoculated rabbit may be artificially raised until it reaches 110° F. in its medulla oblongata, but the virus is in no degree modified by this heat, which cannot be endured, but speedily kills. The time is too short for sterilization. The temperature in the human medulla oblongata may be raised to 106° F. by exposure of the individual to dry heat of 180° F., which cannot long be safely endured, nor would it sterilize.

In the nervous system, a morbid histology in rabies is evident, but it is not absolutely pathognomic of the disease. It may be also present in other diseases, which, however, are uncommon in those animals in which rabies is common. In the *Annales de l'Institut Pasteur,* M. V. Babes of Bucharest, in April, 1892, described, in the medulla oblongata and cord, pallor of cell protoplasm, vacuolation, pigmentation and nuclear

division, hyaline degeneration of nerve-sheaths and vessels and small-cell exudate. An interesting and characteristic change is observable in the histology of the nerve ganglia, especially the intervertebral. Pathology in this country is indebted to Drs. Ravenel and McCarthy of the University of Pennsylvania for a most instructive exposition of these changes (Rapid Diagnosis of Rabies, *University Medical Magazine,* Phila., January, 1901), which consist in the breaking up of the cells bordering the capsules of the nerve-cells, which themselves are overlaid by these dispersed neuroglia cells. In many parts, the nerve-cells have disappeared. The section is bestrown with small cells.

With such histology, rabies is almost surely present. Without it, rabies is almost surely absent. In either case, treatment should be given. Absolute certainty at present is an unattainable desideratum.

In the preparation of the cords and in the treatment of patients, the technique of the Institut Pasteur, Paris, has been strictly adhered to, from which methods there are deviations. Of these the attempt to preserve cords and their virus in glycerin is very unreliable. If the glycerin is

neutral and remains so, the cord may retain its virulence; but, if the glycerin undergoes change, especially if it become acid (which it is liable to do), the virus will be destroyed, and the cord rendered sterile, inert, useless.

RABIES.

Synonyms.—Lyssa, Hydrophobia; Fr., *Rage;* Ger., *Hundswuth, Wasserscheu.*

HISTORY.

Democritus of Abdera, the so-called laughing philosopher, in the fifth century B. C., is accredited with the earliest account of rabies. He regarded it as an inflammation of the nerves, a severe, spasmodic disease, like tetanus. It did not excite his risibility either derisively or incredulously. His opinion was like that of Celsus, who (B. C. 21) wrote: "It is a most miserable kind of disease, in which the sick man is at the same time tormented by a dread of food and water, in which condition hope is reduced to a narrow limit." Aristotle, fourth century B. C., refers to rabies in the dog and its transmission to other animals when bitten. Hippocrates, contemporaneous with Demetrius, makes no mention of rabies, not because he did not know of it, but no case was in his personal knowledge. Unlike philosophy, medicine cannot dispense with experi-

ence. For like reason Trousseau (1850) discusses the disease, but Graves (1848) does not. The description of the former is unsurpassed in the vivid actuality with which the clinical phenomena are presented. It was reserved for Pasteur, in 1882, to treat the disease with definite scientific accuracy.

Ancient Authorities.—Most of the ancient classic writers, historians, philosophers, poets, and physicians refer to rabies. Xenophon, 445 B.C.; Ovid, 107 B.C.; Virgil, 70 B.C.; Horace, 65 B. C.; Plutarch, first century; Galen and Cœlius Aurelianus, 131 A. D.; the former styles rabies the worst of all diseases. With Rhazes (922 A. D.) and Avicenna (1036 A. D.), succeeding authors contributed nothing of importance to this disease.

Early Modern Authorities.—Centuries elapsed before the earlier modern writers resumed the investigation of rabies. Boerhaave (1700 A. D.) and Van Swieten (1771 A. D.) refer to pain in the bitten part and neighboring regions as premonitory, which sometimes like an aura radiates along the nerves. The latter makes the important observation that in a case of rabies in man " death was not preceded by convulsions

or struggles, but as if universal paralysis caused death." John Hunter (1776 A. D.) is responsible for the statement that only 5 per cent. of those bitten became rabid. Magendie and Bouchet (1813) "produced rabies in dogs by inoculating the saliva of a rabid man, afterwards the experiment was confirmed by Reynault at Alfort." Marochetti of Moscow (1820) asserts that in all cases in which medical treatment has not been early applied small knots appear under the tongue at the openings of the submaxillary glands, and that by the use of a probe a fluctuating fluid, which is the hydrophobia poison, may be perceived. Fifteen cases applied for cure on the same day and 12 exhibited the knots. They usually appear within the third and ninth days after the bite. Marochetti examined the mouth once or twice a day, and as soon as these knots or pustules appeared they were opened and cauterized with a red-hot needle; after which the patient gargled frequently with a decoction of broom. If the knots are not opened within 24 hours the poison is reabsorbed and the patient dies. Thirty-eight patients were thus cured. Sixteen were well three years afterwards (*Westminster Review*, 1824).

Morgagni doubted the efficacy of the above-described treatment. Trousseau, as late as 1861, regarded these statements as worthy of attention. Dupuy (1824) states that uniformly he has found the spinal cord softened, diffluent, and of a deep yellow color, especially in its lower portion. Youatt (1850), who is reported to have relied on nitrate of silver as a caustic, is said to have been bitten seven times with impunity, and finally to have died of this disease in spite of his own remedy. M. H. Bouley records that only 20 or 25 cases of rabies occur annually in a population of 36,000,000. Watson (1885) asserts that the Earl of Richmond died of rabies from the bite of a tame fox. Virchow and von Ziemssen (Bollinger's article) "reject the theory of spontaneous development" (1875). During this period it was already known that the saliva or the nervous tissue, hypodermically introduced, could propagate rabies from man to the lower animals as well as from these to one another.

Recent Modern Authorities.—The epoch of recent accurate investigation dates from 1880. It may be regarded as the capstone of Pasteur's mental monument. Around the shaft are imperishably engraven the names of Roux, Cham-

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berland, Grancher, and, as the master desired, that of Thuillier, who, before its completion, died of cholera in Egypt; Duclaux, founder of the *Annales de l'Institut Pasteur,* and since 1895 Director of the Institute; Metchnikoff, Director of Bacteriological Department, Nocard, Babes, Strauss, Calmette, Yersin, Gamaleïa, about the year 1882, Galtier (1881). The book of Renaud Suzor in English (1887) is an admirable presentation of the whole subject at that date. Victor Horsley's experimental demonstration of rabies in the deer of the English parks is an example of accurate work. In Italy were Tizzoni, Cantani, and Bruschettini (1897).

GEOGRAPHICAL DISTRIBUTION.

The regional prevalence of rabies is a field fertile in ill-ascertained, conflicting assertions. Virchow is inclined to regard Greenland, Denmark, the whole of Africa, and parts of Asia and South America as exempt. Bondin (1861) thinks it rare in the tropics. On the contrary, in 1860, it was epizootic in Greenland at 25° below zero. In Constantinople, often referred to as free from the disease, it prevailed exten-

sively in 1839. It occurs in Egypt notwithstanding the denial of Larrey. "In Missouri and Ohio, United States, in 1860, so many cattle were destroyed by this disease that the owners sought reimbursement from the government." It is said to be rare in California. In London between 1603 and 1728 no cases are noted in the mortuary statistics, subsequently cases are regularly reported. In Hamburg it was epizootic from 1851 to 1856, when 600 authentic cases occurred. In Saxony between 1853 and 1867 there were 807 genuine or suspected cases. In Bavaria from 1863 to 1867 among 275,000 dogs there was a yearly average of 800 cases, genuine or suspected. The foregoing account is from Bollinger in von Ziemssen's Encyclopædia, who asserts in italics that no land or country is free from hydrophobia.

The seasonal prevalence of rabies is assigned by vulgar belief to mid-summer or dog-days; probably an outcome of association with the ascendency of the dog star (Sirius). "In respect to the seasons, no very decided preference is evinced for any particular period. It may rage at any time, but appears to be slightly more prevalent during the spring and summer

months" (Bollinger). The appended table from Suzor does not bear out this statement:

June, July, and August	14
March, April, and May	35
September, October, and November	25
December, January, and February	14

In my own knowledge two were in February, one in January, three in December. There is some evidence that prolonged heat may prolong the incubative stage, and some that it may postpone the time of death. J. M. Byron, M D. ("Researches in the Loomis Laboratory," New York, 1890) states that a cord in incubator at 40° C. for eight days produced when inoculated into rabbits marked symptoms of rabies, but the animals did *not* die. "Moderately high temperatures, acting in experiments in tubes, have an attenuating influence on virulent cords; atmospheric temperature influencing inoculated animals seems to affect the virulence, but further experimental data are needed before deriving any definite conclusion." Dr. Acosta, Director of the Antirabic and Bacteriological Institute, Havana, Cuba, reported to Dr. Byron the same irregularities in experimental rabies during the hot summer months.

RABIES IN ANIMALS.

The animals subject to rabies are among the Omnivora, Carnivora, Herbivora, Rodents, and it is asserted Saurians and Batrachians, these perhaps without adequate proof; man, dog, cat, cow, horse, sheep, goat, swine, deer, wolf, jackal, and allied species. Rabbits and guinea-pigs are the experimental subjects of this disease. There is no mention of its prevalence among lions, leopards, wildcats. It is probable that the disease could be experimentally conveyed to them. It can be so transmitted to the domestic mouse, which is very susceptible to the disease. It exhibits the signs markedly. The impairment and disorder of motility is very evident when this active little animal is so situated as to enable it to exercise freely. A small cage with a compartment opening into a light tin and wire bar wheel so constructed as to revolve easily affords the mouse an opportunity to display its agility. It delights in turning the wheel, which it does rapidly and with exact coördination, never missing to place its foot upon the bar. The onset of rabies is shown in the slower movement, in missing the bar, in thrusting its extremity between the bars

and stopping often to rest. From this condition the disease develops in the direction of quiet or of excited rabies. In the former the mouse tends to rest. If undisturbed the disease is not evident, there being only a degree of tremor; but, forced to move, the usual incoördination becomes manifest. It attempts to revolve the wheel, frequently missing the bar. At a further stage it turns the wheel with its fore limbs, the hind ones being extended, motionless, and dragged outstretched backwards, paralyzed. In the excited form there is a tendency to restlessness; slight disturbance causes it to stagger from one compartment to the other. It struggles to revolve the wheel, falling from side to side and over and over. Recovery even in this advanced stage is not impossible in the mouse. In the rabbit it has not been observed to occur when the symptoms have fully declared themselves.

So characteristic are the signs of this disease in the mouse that, except for the purpose of exhaustive demonstration, the transfer from mouse to rabbit is supererogative. It is readily transferable as the cases cited show. The mice were injected in the subcutaneous tissue at the root

of the tail. A piece from the floor of the fourth ventricle, of the medulla oblongata of a rabid rabbit, of the size of 2 cm., was rubbed up in 1 c.c. of bouillon. Of this 5 minims were injected into the back at the junction of the tail, with an ordinary hypodermic syringe.

In the return control experiments the medulla oblongata of the mice hypodermically injected was used to inject the trephined rabbits subdurally.

The source of the material in all cases except three was the medulla oblongata of rabid rabbits. These three exceptions, which did not develop rabies, were injected hypodermatically —one from the medulla oblongata of a rabid hen, one from the medulla of a rabid mouse, one from a culture from the medulla oblongata of a rabid man. Rabic virus in a hen, the temperature of which is 108° F., becomes sterile and cultures producing rabies are unknown, so that two of these cases must be classed with accidental deaths. The total number of mice was 31: Accidental deaths, eight; regular rabies, 17; recovered, one; convalesced and relapsed, one; escaped the disease, four. Subtracting accidental deaths from the total reduces the num-

ber to 23—19 of which took rabies. If this is a maintainable average, then 82 per cent. of mice take the disease when hypodermically injected.

As a control to these experiments 17 rabbits were trephined and inoculated with the medulla oblongata of the rabid mice and all died of rabies. Of these several are noteworthy. Rabbit No. 147 was trephined and injected subdurally with some of the medulla of mouse No. 6 rubbed up in bouillon. Mouse No. 6 had been injected at the root of the tail hypodermically with the medulla of rabbit No. 121, and developed rabies on the ninth day. Rabbit No. 140, injected subdurally from mouse No. 2, developed rabies on the ninth day. Rabbit No. 118, trephined from the medulla of mouse No. 1, had advanced rabies on the eleventh day; mouse No. 2, injected hypodermically from the medulla of this rabbit, developed rabies on the eighth day. Rabbit No. 117, injected subdurally from the medulla oblongata of mouse No. 1, had advanced rabies on the eleventh day.

EXPERIMENTAL INOCULATION.

The presence of rabies in an animal and the susceptibility of an animal to rabies must be experimentally demonstrated. The material preferably used is a portion of the medulla oblongata of the suspected animal, which is introduced by injection beneath the dura mater. The anterior chamber of the eye may be used, the ear vein or other, also the nerves may be injected. The surest method, very rarely failing, is the subdural cerebral lymph space. This involves perforation of the skull, which is usually done by trephining. Pasteur invented this method, without which failure to inoculate is so frequent that experiments frequently miscarry. Two-thirds of the animals artificially inoculated by other methods with saliva are claimed to take the disease, which is also the proportion when dogs are bitten by rabid dogs (Youatt). From causes that cannot be explained inoculation hypodermatically often fails. Nine attempts by Hertwig to inoculate a poodle failed. Pasteur observed this natural immunity. "Are any dogs refractory to rabies, or have those apparently so had a mild attack and recovered?

Dogs and rabbits may have a mild attack and recover, but never after the advent of acute symptoms." "We at present have in our possession four dogs which are not susceptible of taking rabies whatever method of inoculation be used and whatever also the virulence of the rabid material employed."

Method of Trephining.—The appliances for trephining are a board 77 cm. long by 36 cm. wide, having two holes at each side of either end 7 cm. apart and of 1½ cm. diameter. Through these apertures narrow flat or round leather straps are passed and secured, having previously been fastened to the legs by a slip knot. The board previously described has strips fastened to the bottom so that it is elevated above the table on which it is placed; the strips are 12 cm. high. The zinc or slate-covered dissecting table is convenient to place the rabbit board upon. A smaller board, 60 by 36 cm., is used to hold the instruments. The straps should be placed on the legs first, then the hind legs fastened to the board; up to this point the rabbit has not been disturbed and remains quiet. Now the straps on the fore legs are seized and the rabbit stretched out by pulling on them, after

which they are passed through the orifices and made fast. The hair between a line drawn transversely through the ears and eyes is cut off with scissors and washed with a 3 per cent. solution of carbolic acid. No anæsthetic is required; the animal does not cry out, and evinces no sign of pain. A cut one inch and a quarter long is made with the knife or scissors, longitudinally, through the skin in the middle of the space at the top of the head between the lines above named. A blepharostat keeps the incision apart, and the sublying tissue is scraped away so as to expose the bone a little to one side of the median line. The trephine has a diameter of 5 mm., and a ring guard which is set at 2 mm. from the cutting end of the crown; the trephine may be a bit fastened in a revolving drill handle or a simple hand trephine made of metal rod 17 cm. long. The button of bone is removed with a tenaculum and the dura is exposed, and an ordinary hypodermic syringe is used to inject three or four drops of the rabic emulsion beneath the dura. If the perforating end of the needle is curved almost at a right angle for a space of 4 mm. it facilitates its introduction, but is by no means indispensable. The wound is closed by

interrupted suture (three generally are sufficient) and then sealed with collodion. The ordinary suture needle can be used, but the risk of sticking the hand is lessened if the needle has a fixed handle, the other extremity terminating in a spear with a slit in its side, which is opened and closed by pushing a button. It is passed through the skin closed, then opened, the thread inserted, when it is again closed and withdrawn. Of course, all the materials and instruments have been sterilized, and during the operation are placed in a pan of 3 per cent. carbolic acid. Take the rabbit by the skin of the middle of its back, raise it somewhat from the board, and loosen the fore limbs first. The rabbit is then placed in a box properly labelled. Wire cages are generally used, but if the floor be of asphalt or other cement, a box without a bottom, having a wire grating for a lid, with a bed of sawdust or straw, is more convenient to keep clean.

ETIOLOGY.

The intimate cause of rabies remains unknown to this day. Notwithstanding the constant, ample supply of material, research is still at fault. Pasteur himself, for a brief time, thought that he

had discovered the bacillus of rabies in the saliva of a child that had died of this disease. The disease produced was septicæmia, as finally determined, but pending this Pasteur "expressed the idea that this new disease might possibly be the form assumed by human rabies in the lower animals" (1881, Suzor). Dr. A. Bruschettini, of Turin, claims to have discovered the cause of rabies in a small, short, thick bacillus, with a clear zone in its centre. A bacillus of this description may be found in the medulla oblongata of rabid dogs, and this grown in emulsion of the brain, removed and regrown to the fifth generation is claimed to have produced rabies in subdural inoculations of rabbits, and the brain matter of these to have in like manner produced this disease in other rabbits (*Centralblatt für Bacteriologie,* Band XX, 1896, Nos. 6 and 7).

Alongside of this article, in the same journal, Dr. G. Memmo, of the Hygienic Institute, Rome, claims to have discovered the cause of rabies in a species of blastomycetes from the brain of experimentally rabid rabbits, also from the brain of a child that had rabies from a dog-bite. "This organism intraperitoneally injected into guinea-pigs in 11 to 20 days causes paresis of

hind limbs, extending rapidly, and death in about 24 hours, often preceded by clonic convulsions. The virus from the abdominal cavity produces some symptoms in other guinea-pigs. Dogs injected subdurally or subcutaneously become thin in seven to eight days, snappy, foam at the mouth, and are paralyzed in the limbs. This disease could be transmitted from dog to dog but not to guinea-pigs" (Gorman Sims Woodhead in Albutt's "System of Medicine"). Both of these investigations cannot be right, and neither has received general scientific confirmatory demonstration and acceptance. The bacillus described by Bruschettini is like that of rabbit septicæmia, except that it is coarser, which the bacillus of rabbit septicæmia also becomes when grown in certain media. Many of these bacilli with clear centres and bipolar staining are decomposition organisms, the clear centre being a gas vacuole, and sometimes a surrounding clear space of like nature deceptively resembles a capsule. It has been suggested that rabies is a modified septicæmia with a predilection for the nervous system. The writer has never been able, except in the case of one rabbit, to get a prolonged incubative stage like that of rabies in

experiments with septicæmia virus; moreover, in this case all the marked symptoms and signs in sequence so characteristic of rabies were not present.

That the well-known bipolar staining bacillus of rabbit septicæmia may be found in the medulla oblongata of a supposed rabid dog the following experiments demonstrate. In the course of an investigation regarding the etiology of rabies it became necessary for the purposes of control to use the medulla oblongata of a number of dogs for subdural inoculation. One object of these controls being the determination as to whether any other disease than rabies could give rise to like signs and symptoms, it was requisite to use sick dogs; therefore the dogs used had died or had been killed because of suspected rabies. The bacteriological developments of dog No. 17 are noteworthy. This dog was a yellow cur weighing 20 pounds. Shot, and skull crushed. It had attempted to bite a number of persons; it bit other dogs and took refuge in a stable and bit a horse.

Post-mortem examination, September 22d, 1893: Inspection, skull crushed and brain torn: mouth pigmented (a sign of no value as regards

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rabies; dogs' mouths are often pigmented). Cheeks and under surface of tongue bluish vascularity. Bits of coal and splinters in the mouth (a sign of not much value in a dog that obtains his sustenance from the garbage box). Section: cervical lymph glands enlarged and blood effused into them. This sign is important as indicating toxic infection, and is present in rabies in the lymph glands at large in the body, macroscopically or microscopically. Medulla oblongata under surface very vascular. Larynx somewhat red, and the mucosa of the laryngeal ventricles protrudes. Œsophagus pinkish; stomach contains hair, straw, grape skins, feathers. Heart blood coagulated. Lungs ooze a sanious serum. Liver hyperæmic; spleen reddish, firm; weight, 19.4 gm.; length, 16 cm.; width at wider end, 4 cm.; at other end, 1 cm.; thickness, 5 mm.

Cultures from medulla oblongata, spleen, lymph glands, and parotid grown in gelatin. Cultures from cervical lymph gland in bouillon were placed in thermostat.

September 24th, 4 p. m.: Gelatin liquefied contaminatively (which the organism about to be referred to does not do). Cultures in bouillon are very fetid and exhibit lance-shaped cocci

(bacilli); also bacilli with clear interspace and bipolar staining, and curved chains of five or six. There is also a short, thick bacillus in gas vacuole, which is present in ordinary putrefaction. The cultures from gelatin are less gross than those from bouillon and exhibit more clearly the unstained intermediate space. The odor of gelatin cultures is as fetid as those in bouillon. The above applies to the cervical lymph glands of dog No. 17, and to the heart blood of rabbit R in gelatin, below referred to (rabbit R was trephined and inoculated from the medulla oblongata of dog No. 17). This bacillus, slender, with rounded ends, bipolar staining, and clear interspace, varies in size in the same media, differs in size in different organs and structures. It is the well-known bacillus of rabbit septicæmia, and further reference to its morphology and mode of growth is out of place on this occasion. Lenses of good definition are indispensable, because the organism is often very short and the clear interspace very narrow, easily mistaken for juxtaposed cocci. The ordinary carbol-fuchsin stain, if allowed to remain but a few seconds on the cover smear, gives satisfactory results. The following are the details of this experiment:

On September 22d, 1893, three rabbits were trephined and 1 c.mm. of the medulla oblongata of this dog was injected beneath the dura. On the same occasion three rabbits were injected hypodermically in the lumbar region with 1 c.c. of a bouillon mixture of medulla oblongata of this same dog. These rabbits were designated K, T, and W, the trephined rabbits by the letters R, W, and X. Rabbit R died on the third day, rabbits W and X on the second day. Rabbits K and W died on the second day, and T on the fourth day. Cultures from the heart blood of all these animals exhibited the organism described above. Cultures from the heart blood of rabbit R, which was trephined and inoculated from the medulla oblongata of dog No. 17, injected hypodermically into rabbit Y killed it in one day. This ends the trephining experiment. Cultures from the heart blood of rabbits K and T (which rabbits were directly injected with the medulla oblongata of the dog) killed rabbit T′ in one day. This ends the experiment with the medulla.

Referring to the post-mortem examination of dog No. 17, it will be noticed that its cervical lymph glands were enlarged and blood effused

into them. Cultures from the glands give the following interesting results: 1 c.c. of the bouillon culture injected into rabbit Z killed it on the second day; this is the first remove from the dog. Cultures of the heart blood of rabbit Z in Dunham's fluid injected into rabbit Z′ killed it on the second day. Rabbit T′ was identically injected and also died on the second day. These rabbits are second removes from the dog. Guinea-pig H, injected with 1 c.c. cultures of heart blood of rabbit Z in Dunham's fluid, died on the sixth day. Guinea-pig G, injected with 1 c.c. culture of heart blood of rabbit Z in gelatin, died on the sixth day. These guinea-pigs are second removes from the dog. Mouse A, injected with 5 minims of culture of heart blood of rabbit Z in Dunham's fluid, died on the third day. This mouse is second remove from the dog. Cultures from the heart blood of the mouse A in Dunham's fluid injected into rabbits S′ and L′ killed them on the third day; this is the third remove from the dog. Cultures from the heart blood of guinea-pig G (above mentioned) in Dunham's fluid injected into rabbits R′ and Q′ killed them on the second day; this is the third remove from the dog. Cultures from

the heart blood of this same guinea-pig G injected into pigeon A killed it on the seventh day; this is the third remove from the dog. Rabbit N′ was injected with the culture of the heart blood of pigeon A and died on the second day; this is the fourth remove from the dog. The experiment ceased with the fourth remove from the dog. Another pigeon (B) was killed by an injection of the culture of heart blood, this being also the fourth remove from the dog through mouse A. All of these animals, as well as the cultures, exhibited the organism described above. Two white rats, three times injected, remained immune. It is to be noted that when other animals than rabbits have been killed by culture, other rabbits have been killed by cultures from these animals, constituting a return control experiment.

The signs and symptoms of this disease (septicæmia) in the rabbit ante-mortem and post-mortem are markedly characteristic and can never be confounded with those of rabies. The ante-mortem signs are somnolency and dyspnœa. The animal sits with its ears turned back upon its body, its flanks panting laboriously, its eyelids constantly closing. The alvine evacuations

are pultaceous. The temperature may rise to 106° F., which is one or two degrees above the normal maximum; this rise is very transient, rapidly falling three degrees below the normal temperature of the rabbit; the normal minimum temperature is about 100° F. Usually these animals die quietly; exceptionally, convulsed. A constant post-mortem sign is the pale, salmon-colored, bloodless, anæmic, collapsed lung. The spleen is sometimes enlarged; the liver friable. The intestine has exhibited no lesion except increased vascularity. The site of the injection usually shows increased vascularity, exceptionally sloughing.

Of great interest is the fact that this organism of rabbit septicæmia was obtained from the medulla oblongata of a probably rabid dog. Had these rabbits recovered from the septicæmia they would have died of rabies, and a causal relation might have been erroneously attributed to this organism.

The disease produced by this bipolar bacillus is totally unlike that produced by the virus of rabies. The incubation in rabies, even when the virus is fixed, is six days. The rabbits infected with the septicæmia organism became sick in a

few hours and died about the third day. Rabbits with rabies from the dog immediately without intervening experimental transmission do not exhibit rabies until from the twelfth to fifteenth day, usually the latter. Rabid rabbits survive three, four, and five days after its development. Muscular incoördination and paralysis are marked; they are absent in septicæmia. There is, however, a disease known as pseudo-rabies, in which the incoördination and paralysis are exactly like those of true rabies, and may, like true rabies, be produced by subdural inoculation of the medulla oblongata. This is also an idiopathic disease of rabbits and may supervene without inoculation, so that a confusion of causation might arise during experimentation. But inoculation of the rabbits would exhibit the characteristic signs: the short incubation and easy cultural reproduction.

Though the *causa causans,* the ultimate cause, of rabies eludes detection, the proximate cause is readily demonstrable and can be indefinitely propagated experimentally. When naturally imparted there is tendency to extinction. " Magendie got a first mad dog to bite a second healthy one; this in turn, when mad, a third one, and

so on. The periods of incubation became longer and longer, and the fourth or fifth dog failed to take the disease" (Suzor). Galtier (1881) produced rabies in rabbits by the insertion of pieces of the brain and medulla of rabid dogs under the skin. That the cause of hydrophobia, rabies, is seated in the nervous system is constantly proven. Especially is the medulla oblongata virulent, and this is the part used in experimental inoculation. The Paris virus from the Institut Pasteur in use at the laboratory of the College of Physicians and Surgeons, in Baltimore, was received in neutral glycerin, which is said to impair its virulence for only the first two or three passages. This has not been my experience; the virus in glycerin seemed inert on one occasion, and failed to produce rabies in three rabbits trephined and inoculated therewith. There is difficulty in fixing the virus when in this menstruum, and this has also been the experience in the New York Board of Health laboratories. A series of very interesting experiments upon the frequency of rabies in the human being made by the late Dr. J. M. Byron, of the Loomis Laboratory, New York, has this element of vitiation, and in addition there seems to have been a bias in the direction of infre-

quency. This experiment shows that decomposition exerts little or no influence on rabic virus. Cords in an early stage of decomposition, when nothing is grossly noticeable except a little softening, promptly kill when inoculated subdurally or hypodermically. But the same nerve matter when stinking rotten may often be used with impunity, and successfully, in imparting rabies. The Paris virus at this laboratory at this date, May 30th, 1898, has reached the four hundred and ninety-ninth remove,[1] that is, it has been passed from one rabbit to another until it has reached this number of passages; but as two rabbits are inoculated subdurally each time it has given this disease to at least 998 rabbits. This Paris virus started from the medulla oblongata of a rabid cow in 1882. Another virus in use at the above institution was introduced by the writer October 5th, 1893. Coincidentally, this virus also started with the medulla oblongata of a rabid cow received from Wm. R. Tatum, D. V. S., Brighton, Md. This virus has been passed from rabbit to rabbit until 153 removes have been reached (May 30th, 1898).[2] The number of rabbits that have uninterrupt-

[1] July 20, 1909, 800 removes.
[2] July 20, 1909, 500 removes.

edly taken this disease in these experiments is 760. In the earlier experiments more than two rabbits were used at each subdural inoculation. A rabbit will live about 12 days after inoculation, so that about 30 passages may be made each year. Inoculating with the medulla oblongata of a rabid horse the disease has been passed from rabbit to rabbit to the tenth remove. Sixty rabbits were the subjects of this experiment. The disease has been passed three times from the human animal to the rabbit, using in this experiment 14 rabbits and stopping at the second remove. If a fixed virus were obtained starting from the medulla oblongata of a human being there would probably be no appreciable difference. The antitoxin of rabbit serum is stated to be more effective in immunizing rabbits than that obtained from a different species.

Rabies can be passed from man to the lower animals with ease. Contrary statements in standard works by reputable authors as late as 1888 are surprising. Not only can the materies morbi be readily passed from human beings to other animals, but the source of the virus can, to a certain degree, be determined; that is,

whether the virus is a fixed laboratory virus or a virus immediately from the animal—"*rage de rue.*" This was the grave question that confronted Pasteur when the first death from rabies occurred during treatment by his method. The profession and the public knew that rabic virus was injected hypodermically into patients. Dr. Peter, of Paris, demanded the closure of the Institute, declaring that this treatment produced rabies. When Louise Pelletier, aged ten years, died of rabies on the fourteenth day after termination of the treatment, having developed this disease 11 days thereafter, it became necessary to show whether she was killed by the treatment or by the disease. Pending this determination must have been a moment of stupendous suspense. "It was easy to know," remarks Pasteur. The demonstration of the cause from which the death of this child resulted, and its origination, was a matter strictly of experimental investigation dependent upon the following data: The virus, immediately from a rabid animal (the medulla oblongata being used), injected subdurally into the cerebral lymph space, produces rabies in the rabbit at or about the fifteenth day. The remote fixed virus of the laboratory

produces rabies in about six days. An emulsion of the medulla oblongata of this child, subdurally injected into two rabbits, did not develop rabies until the eighteenth day thereafter. The medulla oblongata of these rabbits (they having been allowed to die and not prematurely killed), injected in the manner above described, into other rabbits, caused them to develop rabies in 15 days. The cause, then, of this child's death was the virus of rabies as it exists naturally, not this virus as made more virulent by progressive propagation experimentally.

Two points in this case are noteworthy. The child developed the disease on the eleventh day after the termination of the treatment. It requires 15 days after termination of the treatment to complete immunization; therefore in this child the full benefit of the treatment had not been received. Cases of this description cannot be strictly accounted failures of the treatment. The second factor requiring attention is that the virus was inoculated into two sets of rabbits. The first set, consisting of two rabbits, was inoculated from the medulla oblongata of the child. When these rabbits died a second set of rabbits were inoculated from them, be-

cause in the first passage of the virus from one species to a different species the period of incubation in the latter is not uniform, but is variable as to duration. In the passage through the second set the virus, passing from and through the same species, exhibits by its period of incubation its grade of virulence. In the words of Pasteur: "The method rests essentially on the following facts: The rabbit inoculated under the dura mater, after trephining with the spinal marrow of an ordinary mad dog, is always affected with rabies, and takes the disease after a length of incubation averaging about 15 days. After a number of passages through rabbits varying from the twentieth to the twenty-fifth, the incubation falls down to eight days, which remains the normal incubation time for the next 20 or 25 passages. Then it reaches an incubation of seven days only, recurring with striking regularity up to at least the ninetieth passage; at this point there is a slight tendency towards a shorter period of incubation than seven days." The ultimate diminution of the period of incubation seems to be six days. A fixed virus produces rabies in six days, when subdurally inoculated.

The following cases are recorded because of intrinsic interest; further, because they in some degree illustrate the rigorous, exhaustive causal demonstration that science demands.

These cases have been designated as the Baltimore cases of rabies. On December 1st, 1896, a large dog, cross between St. Bernard and mastiff, bit eight boys in Baltimore City Annex. Of these boys four died of rabies within 36 days after having been bitten, and within 19 days after the termination of treatment by the Pasteur method in New York. The bites were severe in character and situated on the bare face and neck.

1. Wilson, aged 11 years. Seat of bite on face over left eye. Not cauterized. Date of discharge, December 17th, 1896. Date of bite, December 1st, 1896. Date of first treatment, 42 hours after bite. Date of death, January 5th, 1897, 18 days after treatment.

2. Perry, aged 16 years. Seat of bite on cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, 77 hours after bite. Date of death, December 26th, 1896, eight days after treatment.

3. Eppers, aged 15 years. Seat of bite, back of neck. No efficient cauterization. Date of discharge, December 17th, 1896. Date of first treatment, 50 hours after bite. Date of death, December 26th, 1896, nine days after treatment.

4. Henry, aged eight years. Seat of bite, left cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, 77 hours after bite. Date of death, December 21st, 1896, three days after treatment.

A boy named Kiel was bitten on the ear, but through an ear warmer, and therefore must be excepted from the class of bites on bare parts. All bitten on the bare face and neck died; all others escaped. They are:

5. Perry, aged 18 years, brother of No. 2, bitten on the arm.
6. Ashley, aged ten years, bitten on arm.
7. Buhl, aged 14 years, bitten on arm.
8. Kiel, Joseph, aged 15 years, bitten on ear through an ear warmer.

The foregoing is a necessary preliminary statement. The chief object of this communication is to bring before the medical profession the experimental details proving that the dog had rabies, and that two of the boys, Henry and Eppers, also had it. In the other two cases a post-mortem examination was not obtainable. Also that the virus was from the dog and not from the treatment.

The following is the post-mortem examination of the dog, December 2d, 1896, 2 p. m.: Cross between St. Bernard and mastiff: yellow, with white neck; weight, over 100 pounds; shot after having bitten eight boys, chickens, and dogs. Hard palate, dark bluish in color. Rigor mortis marked. Brain soft. Medulla oblongata soft, and softening around central canal of spinal

cord. Lungs ooze freely bloody froth. Kidneys, dark red cortex. Bladder empty. Liver normal. Spleen normal. Stomach contains pieces of wood and stone, straw, horsehair—mane or tail. Larynx, blood in, from wounds in mouth. Trachea, blood in, from wounds in mouth. Heart normal. There is an effusion of blood in the cervical lymph glands.

December 2d, 1896, 2 p. m.: Trephined three rabbits and injected beneath the dura 3 minims of an emulsion of the medulla oblongata of this dog in sterilized water. These rabbits developed rabies, two on the fifteenth and one on the seventeenth day.

December 19th, 1896: Killed rabbit C on seventeenth day after inoculation. Trephined and injected the emulsion of its medulla oblongata in sterilized water subdurally into rabbits D, E, and F. Amount injected, 5 minims. Rabbit D died accidentally. E and F developed rabies on the sixteenth day.

Thus five rabbits have been given rabies from this dog; three immediately from the dog, two from one of these rabbits, this rabbit having been killed in order to stamp a suggestion of putrefaction as a fallacy. The latter experiment

proves the disease to be an infectious neurosis, not a traumatic degeneration.

Experiment demonstrating that Robert Henry, aged eight years, of Baltimore, died of rabies. He underwent Pasteur treatment in New York, arriving there about December 4th, 1896, and returning to Baltimore on the night of December 18th, 1896, being then sick. He died of rabies December 21st, 1896, 5 p. m. He had been bitten on December 1st, 1896. Post-mortem examination December 21st, 1896, 7 p. m.

December 21st, 1896, 9.30 p. m.: Four rabbits were trephined and injected subdurally with emulsion in sterilized water of the medulla oblongata of the boy Henry. Amount injected, 5 minims. One developed rabies on the fourteenth day, three on the fifteenth day.

Experiments demonstrating that the boy Henry died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit was a specific infection, and not a traumatic degeneration (neuritis, ascending or descending).

January 7th, 1897, 2 p. m.: Rabbit K trephined and subdurally inoculated from medulla

oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally inoculated from medulla oblongata of boy Henry on December 21st, 1896. Rabbit K developed rabies on the fifteenth day.

January 7th, 1897, 2 p. m.: Rabbit L trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896. Rabbit L developed rabies on the fifteenth day.

The rabbit assumes a crouched position. It is unable to sustain its body erect on pelvis and scapula. Motility of limbs impaired, hind legs almost completely paralyzed. Falls over on its sides at intervals. This crouched attitude (paralytic rabies) has been a characteristic feature of the disease in most of these rabbits.

Experiment demonstrating that the cord of rabbit G was not virulent on the ninth day, and therefore the virus with which G was inoculated subdurally was from the dog and not from the treatment.

January 7th, 1897, 2 p. m.: Rabbit M trephined and subdurally inoculated from medulla

oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896.

Rabbit is very unwell, very thin. Sweats about muzzle. Breath fetid like gangrene. This is an intercurrent malady and has no connection whatever with rabies or with the experimental inoculation. This disease occurs not infrequently among rabbits that have been subjected to no experiment. There is reason to regard this disease as infectious. It has as a symptom diarrhœa. There is no disturbance of motility. The rabbit was found dead on the ninth day.

Two rabbits, O and P, trephined from this rabbit, developed no disease whatever. They were under observation for three months. This proves that this disease cannot be communicated by subdural injection of the medulla oblongata; also that the medulla oblongata did not contain the virus of rabies on the ninth day, which it would have contained had the virus been that of the treatment.

Rabbit N was subjected to the same experiments as rabbit M, and died of the same disease on the eleventh day after trephining. It is to

be regretted that no experiment was made to ascertain the condition of the medulla oblongata at this date, as regards the virus of rabies.

Rabbits M and N were in the same box all the time.

Experiments demonstrating that Conrad Eppers, aged 15 years, died of rabies. He underwent Pasteur treatment in New York, arriving there about December 2d, 1896, and returning to Baltimore December 17th, 1896. He died of rabies December 26th, 1896, 12.05 a. m. He had been bitten on December 1st, 1896. Post-mortem examination December 26th, 1896, 11 a. m.

December 26th, 1896, 6 p. m.: Four rabbits were trephined and injected subdurally with emulsion in sterilized water of medulla oblongata of the boy Eppers. Amount injected, 5 minims. Rabbits designated by letters Q, R, S, T. They developed rabies on the sixteenth day.

Experiments demonstrating that the boy Eppers died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit is a specific infection and not a traumatic degeneration (ascending or descending neuritis).

Rabbit U trephined and subdurally injected with emulsion of medulla oblongata, that of rabbit S, which died of rabies on the seventeenth day, January 11th, 1897, after having been trephined and subdurally injected from medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896. Rabbit U developed rabies on the thirteenth day.

Rabbit V trephined and subdurally injected with emulsion of medulla oblongata of rabbit S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896. Rabbit V developed rabies on the fifteenth day.

Rabbit W trephined and subdurally injected with emulsion of medulla oblongata of rabbit S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected with medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896. Rabbit W developed rabies on the fourteenth day.

Rabbit X trephined and subdurally injected with emulsion of medulla oblongata of rabbit

S, which died of rabies January 11th, 1897, seventeenth day after having been trephined and subdurally injected with emulsion of medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896. Rabbit X developed rabies on the sixteenth day.

Comments and Conclusions.—If 100 children had been bitten by this same dog in an identical manner, *i. e.,* severe and numerous bites on the bare head and neck, how many would have likewise perished? A healthy rationality will admit the probability of 80 per cent., 90 per cent., even 100 per cent., of deaths. These cases entirely corroborate all that is claimed by statistics on this point. That is, the mortality of bites of this description is 80 per cent., 90 per cent., even 100 per cent., when not treated by the Pasteur method. But all these were treated by this method with a result as disastrous as if they had not been treated at all. It cannot be claimed that they were not timely treated. All were under treatment in about three days after having been bitten. Greater celerity than this is only very exceptionally attainable. Pasteur institutions cannot be located within three days' journey of everywhere. The only possible expla-

nation is that some factor difficult of appreciation caused an unusually brief incubation and speedy onset of the disease. For the completion of immunization 15 days after the termination of treatment are required. In these cases the disease outran the remedy. If 15 to 20 days are required for completion of the treatment, and 15 days thereafter for the completion of the immunization, then all cases which develop the disease in 35 days are not amenable to treatment. The stage of incubation in 6 per cent. is between three and 18 days; in 60 per cent. it is between 18 and 64 days. Granting the accuracy of these statistics from Bollinger in Ziemssen's "Cyclopedia of Medicine," it may be assumed that 35 per cent. of those bitten, or, confining the statistics to the subjects under consideration, of children at and below 18 years of age, and suffering from multiple and severe and non-cauterized bites on head and face (bare), 35 in 100 cases of this description will fail to be benefited by the Pasteur treatment; 65 cases in 100 cases escape when treated. Granting that 20 in 100 would escape if not treated, then 45 in 100 are saved by the treatment. The foregoing remarks assume that there

has been no defect in the administration of the prophylaxis. The Pasteur Institute, Paris, calls attention to the time limit, but does not plead this statute of limitation. It shows that all the deaths during treatment and at any time thereafter, from bites of the head and face, form only about 6 per cent. But this showing includes all ages, children and adults, and all bites, severe and slight, single and multiple. This is as inexact as the assertion attributed to John Hunter, that not more than 5 per cent. of all cases bitten by rabid dogs develop rabies. This may be true of slight bites through clothing, but it is entirely incorrect as regards severe multiple bites on bare parts, especially the face and neck. There are those who assert that mad-dog bites are very rare, and but very few of the few bitten develop the disease. But when they wish to impugn the Pasteur treatment they cite the present cases, asserting that 50 per cent. of the entire number bitten died of the disease, and 100 per cent. of those bitten on the bare face and neck died. No sufficient number of cases was bitten from which to calculate percentage. They "blow hot and blow cold in the same breath," and mean nothing unless they covertly claim that the

treatment produced the disease. The virus of ordinary rabies, that of the mad dog at large, the street dog, *rage de rue,* when subdurally injected into rabbits, never produces the disease before the twelfth day; rarely before the fourteenth day. On the contrary, the virus of the laboratory, the virus of the rabbit at and beyond the fiftieth remove, develops when subdurally injected into other rabbits in seven or eight days. In the cases under consideration, the virus of the medulla oblongata of the boys produced rabies in the rabbit after about the same incubation as did the virus of the medulla oblongata of the street dog in question. The disease did not, in any of the rabbits, develop before the fourteenth day. Had the virus which gave these boys rabies been that of the laboratory, that which was used in the treatment, then the rabbits which were injected subdurally from the medulla oblongata of those rabbits which had been injected subdurally from the medulla oblongata of the boys would have developed rabies in about the seventh or eighth day. But it has been demonstrated that on the ninth day after injection the medulla oblongata was not even virulent (see rabbit G, *ante*). The use

of a second series of rabbits is necessary for two purposes: First, when the virus is passed from one species to another the incubative stage is variable in the first passage. In these cases—the virus from the medulla oblongata of the boys injected subdurally into rabbits—these first rabbits might manifest the disease at some irregular period, probably a longer interval than its real incubative stage. But when the virus is passed from the medulla oblongata of these rabbits by subdural injection into other rabbits, then these other rabbits exhibit the disease after the stage of incubation normal to the virus. The normal incubative stage of the street virus is about 15 days. The normal incubative stage of the virus of the laboratory which is used in the treatment is about seven days. Secondly, the other purpose necessitating the use of a second series of rabbits is to exclude the effect of traumatism on the nervous system. Very rarely a case occurs after trephining, even when the virus of rabies is not used, in which after a like incubative stage the rabbit develops and dies with signs and symptoms like those of rabies. That this disease and rabies are not identical is proven by the fact that this disease cannot be given from

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these rabbits to a second series of rabbits by trephining and subdural injection of their medulla oblongata; still less can it be so propagated indefinitely, as is the case in rabies, which is a specific infectious neurosis. The other disease is a traumatic inflammation or degeneration. Subdural injections of guinea-pigs or rabbits with emulsion of medulla oblongata of dogs suspected to have had rabies is part of the regular routine work of institutions practising the Pasteur method. Not infrequently the dogs are thus demonstrated not to have had rabies. Patients have been treated and the dog subsequently proven not to have had rabies. If a dog under suspicious circumstances bites persons and is at once killed, it is prudent to give these persons the benefit of the doubt and treat them. They cannot safely delay until the termination of an experiment which lasts over 15 days.

Daily throughout the world institutions administering the Pasteur treatment demonstrate that rabies is a specific infectious (contagious) neurosis, and that no other disease is capable of producing identical signs and symptoms.

In this necessarily discursive manner, the cause of rabies is shown to be something, some

virus, some organism that has been communicated from one being to another. The mode of communication is by contact, and the vehicle, most frequently, saliva. The contact, the conveyance, is usually by the bite of a rabid animal. It is well ascertained that the saliva of a dog may be virulent three days before manifestation of symptoms. " In the rabbit experimentally inoculated (subdurally) the saliva is virulent on and after the sixth day, the virus inoculated being a fixed virus (two hundred and thirty-seventh passage)." The first nerve symptom, incoördination, slight swaying, especially of the head and neck, from side to side when disturbed, in the rabbit, indicates the incipiency of nerve disorder, and the virulence of the saliva seems to be simultaneous. It has been shown that in subdural inoculation of rabbits with the unfixed virus the medulla oblongata is not virulent on the ninth day, but the condition of the saliva at this period has not been ascertained. " A dog inoculated in the anterior chamber of the eye had the rabic temperature rise 11 days thereafter, being 39.3° C.; previously it had been 38° C. and 38.8° C. Saliva at this period injected into the muscles of the neck of a guinea-pig caused it to develop

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rabies in 15 days" (Roux et Nocard). There is obvious danger that abraded surfaces or wounds received in handling, experimentally or otherwise, rabid animals may become inoculated. That it is rare is no proof that it is improbable. If occupation brought human beings into the same association with rabies as with glanders, its transmission would be as frequent and as undoubted in the one as in the other.

Mode of Conveyance of Rabies.—The conveyance of the disease by parasites, fleas, lice, and other pests from the dog, though not demonstrated is not incomprehensible as a possibility. Youatt cites a case in which a man untied a knot in a rope with his teeth and died of rabies, the rope having been used to confine a rabid dog; also another case in which a seamstress had her dress torn by a rabid dog. In repairing it she passed the seam, to flatten it, between her lips; she died of rabies. These cases almost overtax credence. To the class of literature designated as "fairy tales" the following cases belong. Van Swieten "reports that an old woman died with all the symptoms of rabies after a wound inflicted on her by an irate cock. He conjectures that the cock had been bitten by a rabid

fox. If the disease were spontaneously generated in the cock, it is surprising it does not occur more frequently in England, where this irascible bird is trained to fight." The same authority asserts " that a young man died of rabies after having bitten his own finger in a fit of passion." Malpighi " declares that his own mother died of rabies a *few* days after having been bitten by an epileptic." Cases of spontaneous origination of rabies in man are reported by Drs. Barthez and Gintrac. M. Velpeau remarked that there was in these cases no sufficient evidence of the absence of contagion. Some portions of the body, denuded of epidermis, need only be in contact with the virus of rabies. Trousseau, who quotes these cases, remarks " that rabies in the human subject is always the result of inoculation with the virus of rabies." The present-time opinion almost unanimously regards this disease as never now originating *de novo,* any more than does glanders or smallpox. The communication of rabies in coitus is a far more remote possibility than is that of tuberculosis or carcinoma. Is the cause ever congenital? " A cow with hydrophobia (rabies) gave birth to a calf, which developed rabies, although another cow had been

substituted for it to suck from." A rabid cow has to my knowledge furiously attacked its own calf; herein is a source of fallacy. Excellent authority has demonstrated by subdural inoculation of the medulla oblongata of the fœtus of rabid rabbits that rabies existed in them; fallacy in this observation is reduced to a minimum. Milk of rabid animals has thus also been proven virulent. In the above cases the disease may so occur; but that it very rarely does so is the observation of the present writer and also of Professor Perroncito, and Dr. Carita (*Annales de l'Institut Pasteur,* Vol. I). The writer on several occasions has not been able to produce rabies by subdural inoculation from newly born offspring of rabbits with advanced rabies. " The milk and flesh of rabid animals—dogs, sheep, and cattle—may as a rule be consumed by man and animals without any ill effect. Gohier alone states that he has seen hydrophobia produced in a dog by eating the flesh of a dog dead of this disease, also by eating the flesh of rabid sheep. Hertwig made many experiments with negative results. Saliva and mucus from the mouths of rabid dogs were introduced into the stomach and throat of other animals, and they were fed with bread and meat smeared

with rabic saliva, also placed in stalls with dogs which had recently died of this disease, given the same straw, food, washbasins, and chains, all without result." The disease cannot be taken through an intact mucous membrane, protected by its epithelium. Admitting that the risk is slight, still no risk should be run. Admitting, which is not absolutely certain, that an unabraded mucous membrane obviates the entrance of this virus, slight abrasions are easily made and readily escape observation. Youatt held that the virus was absorbed by the mucosa. Rabid animals are thoroughly diseased animals. Their flesh should not be used, even for this reason; nor should their skins be used, though they are less dangerous than those of animals afflicted with anthrax.

Attenuation of Virus.—" The virus of rabies can be weakened, attenuated; when it is passed from the dog to the monkey and from monkey to monkey it grows weaker at each passage. After the virulence has been thus diminished by several passages through monkeys, if the virus be carried back to the dog, the rabbit, or the guinea-pig, it still remains attenuated. In other words the virulence does not go back to the de-

gree it had in the dog. A small number of passages from monkey to monkey suffices to so attenuate the virus that it does not give rabies when hypodermically injected. Intracranial inoculation itself, the never-failing means of communicating rabies, may now remain without effect, while, however, creating a refractory state in favor of the inoculated animal" (Suzor). "The virus of rabies in the lymph sac of the frog becomes attenuated in 15 days, when it becomes a sufficiently strong vaccine for a dog, but not for a rabbit. A mixture of the blood of immune dogs with rabic virus sterilizes the latter in six hours. The frog does not contract rabies, though its migratory cells are to be seen in the nervous substance (gray matter) a few days after the introduction of the rabic medulla into the dorsal lymph sac. M. Pasteur conserves cords by dry air (suspended over caustic potash). It is now known that heat plays the most important part in these experiments, and it may act by favoring oxidation" (Babes, Gerchez, Protopopoff, *Annales de l'Institut Pasteur,* Vol. V).

The virus of rabies subdurally inoculated into the hen has a long incubation, and at the death

of the hen its medulla oblongata will be found to be sterile. It does not give rise to rabies when it is inoculated subdurally into rabbits. The temperature of the hen in the cloaca is 108° F., at which temperature the virus of rabies can be sterilized in vitrio. Rabbits when shaven and exposed to bites of mad dogs are more readily affected (observations of Pasteur and Horsley, Albutt's "System of Medicine," article by Sims Woodhead).

Character and Seat of Bites in Relation to Causation.—In the causation of rabies by bites much depends upon the seat, number of bites, severity, and whether the part be naked or clothed or covered with thick hair. The neck is selected in experimental hypodermic injections of rabic virus, because these injections are more frequently successful in this region than elsewhere. The injections are made deeply into the neck muscles and it is suggested come into contact with the cervical nerves at their exit from the spinal column, and in this way more rapidly and surely reach the anterior columns of the cord.

Numerous, extensive, deep bites on the face and neck are very dangerous. They are estimated

to result fatally in 80-90 per cent.; on hands, 63-67 per cent.; on body, 31-63 per cent., the latter in numerous wounds. Upper extremities (arms), 20-30 per cent. Lower extremities (legs), 21-28 per cent. The general percentage is stated at from 55 to 47. If the wound be cauterized properly and timely, 33 per cent. of those bitten take rabies; if not cauterized, 83 per cent. "Age exerts no appreciable influence on deaths from rabies." Under 20 years, 31 per cent.; over 20, the percentage rapidly goes up to 62.

The following table is from Bollinger:

12	between	3	and	5	years.	49	between	20	and	40	years.
27	"	5	"	10	"	36	"	40	"	60	"
62	"	10	"	20	"	9	"	60	"	over.	

Wide discrepancies in estimates result from difficulty in arranging, in sorting factors. It may be assumed that a bite cannot put the virus more surely or in greater quantity in the body than can a hypodermic injection. If it be assumed further that the guinea-pig is of average susceptibility, then this animal injected subcutaneously in the trunk with a fixed virus gives from 16 to 18 per cent. Injected deeply into the muscles of the neck the percentage is much greater.

The percentage of 50 in deep and multiple wounds of the face and neck is by no means an overestimate. "In what manner or by what course the poison penetrates the body from the seat of the wound is absolutely unknown." This assertion by Bollinger is almost 25 years old, and has received some little elucidation more recently. Any condition that favors contact of the virus with the nerves facilitates the production of the disease, because "the lymph channels of the nerves are more directly in communication with the lymph spaces in the cerebrospinal canal than are other lymph channels," yet the cerebrospinal fluid is not always virulent. It is an observation of Pasteur that sometimes this fluid, though perfectly limpid, produces this disease, and sometimes fails to do so even when turbid. The blood is rarely virulent. Pasteur produced rabies only once from the blood. He called attention to the certainty of infection by intravenous injection. "The nerves are not the sole channels of propagation of the virus from the periphery or surface to the centre." "We (Pasteur says) have on several different occasions inoculated the virus into one of the veins of the ear and then immediately after cut off that

organ with the thermocautery between the point of inoculation and the head. Nevertheless rabies showed itself in every instance, although the thermocautery does not produce an open wound, the whole of the cut surface being burned." Though the blood-vessels themselves are diseased, the blood itself exhibits no change and is rarely inoculable. The virus may preferably go by the way of the lymph route (chemotaxis). The coats of these blood-vessels may be diseased from the lymph channels without and not from the blood within. Perhaps the virus avoids the serum, finds it repellant. Put into the circulation it speedily makes its way out, indicating that blood serum is not a desirable culture medium, either naturally or artificially. That the blood does suffer when in contact with this toxin will be adverted to more in detail in the section relating to pathology.

" If in the dog the spinal cord be cut across, and afterwards one of the nerves of the hind foot be inoculated, the cord below the cut will produce rabies when inoculated, but the part of the cord above the section will be found not to be virulent. The same holds good when a similar experiment is made by injecting a nerve

of a fore limb. When the disease develops slowly as the result of a bite of a limb on one side of the body, the peripheral nerves on the opposite side may also contain the virus" (Woodhead). These experiments indicate that nerve matter is a desirable culture medium, naturally and perhaps artificially, with brain and lymph in combination. The deduction from this experimental sequence is that a part, abounding in nerves and lymphatics, and somewhat close to the spinal origination of the former, is a danger point; which is equally strongly substantiated clinically. The filtrate through porcelain, injected into the dog, causes paralytic symptoms. The entire pathological phenomena are typical of intoxication produced by material loosely designated as toxins: The salivary glands, especially the parotid, and also the lachrymal secretion (which may perhaps cause the ocular inflammation, keratitis, etc.), the mammary secretion, the pancreas, and suprarenal bodies are virulent. Pasteur demonstrated the presence of the rabic virus in the lumbar swelling of the spinal cord occasionally before it was present in the medulla oblongata. The disease has been produced by pieces of the pneumogastric nerve near its cranial

origin and distant therefrom; also the sciatic and submaxillary nerves. The presence of the virus in the peripheral nerve distribution explains in man the strange symptom aërophobia, as does the involvement of the respiratory centre explain the asphyxia not well designated as hydrophobia; it is more uncouth but more in accord with truth to say asphyxiphobia.

Fanciful causes are seasons, temperature, want of freedom and food, age, sex, and race; and restrained sexual indulgence. The best observers hold that these act neither as direct nor predisposing causes. Fanciful scepticism is adverted to as follows by Bollinger: "The denial of the existence of hydrophobia as a specific disease lately by Mascha and Lovinser (1865) has not even the merit of novelty, for the existence of hydrophobia as a disease *sui generis* as well as the existence of a specific virus was denied in France by Bosquillon (1802). According to their views the symptoms are ascribed to fright or to the local injury. Girard and J. Simon (1819) regarded it as an imaginary disease. R. White (1826) regarded hydrophobia as nothing more than an ordinary inflammation of the œsophagus, the stomach, and muscles of respira-

tion. He denied not only its specific character but also its infectiousness. He inoculated several cats, rabbits, and other animals, and finally himself from two rabid dogs, all without result. It is hardly necessary to add that these negative results, as compared with numerous positive results following inoculation, and with simple clinical experience, are entitled to no weight, and are valuable at most only as illustrations of foolhardiness indulged in with impunity." "The spontaneous origination *de novo* of rabies is as incredible as that of smallpox or of spontaneous generation in the abstract. Virchow states that the doctrine of the spontaneous origination of rabies contributed most of all causes to involve in doubt the specific character of the disease. He regards the action of the poison of rabies as comparable to that of ferment, fresh particles of which are constantly being conveyed into the blood from the seat of the inoculation, producing through the medium of the circulation its specific effect upon the nervous system. The resemblance to alcoholic intoxication and to certain forms of mental affection is unmistakable, the poison in each case producing its effects upon the centres of the medulla oblongata and cerebral hemispheres."

The cause of rabies is an infectious (contagious) virus capable of indefinite propagation when inoculated through wounds and abrasions; and also through unabraded mucous surfaces. Age does not of itself markedly affect it, nor does putrefaction in a reasonable length of time. Moderately high temperatures acting in experiment tubes attenuate and destroy its virulence.

Virus Attenuated by Heat.—It has been previously stated that cords in a condition of early putrefaction kill rabbits and other animals by septicæmia, and that the organism is that of rabbit septicæmia; but when putrefaction is advanced, the cord, if a rabic one, develops rabies. "Rabic cords in an incubator for eight days at temperatures of 30°, 35°, 40°, 45°, 50° C., when subdurally inoculated, resulted as follows: 30° C. killed with rabies in about nine days; 35° C. in 11 and 12 days; 40° C. caused symptoms of rabies, but the rabbit did not die; 50° C. were not at all affected." At 86° F. the rabic cords were little if at all weakened; at 95° F. the incubation is markedly prolonged; at 104° F. the disease was mild and recoverable; at 112° F. the cords were sterilized. It is known that 118° F. rapidly renders the rabic virus in tubes

inert. Such is the experimental effect of heat on rabic virus outside the body. Rabic virus in a body having the temperature of the hen (108° F.) is sterilized, but too late to prevent the disease, though its incubation is prolonged. The late Dr. J. M. Byron, of New York (1888), from whom much of the above account is quoted, remarks that the rabbits inoculated with cords that had been exposed for eight days to 40° C. and 50° C. did not acquire immunity, but when subsequently inoculated developed rabies; these cords were not of the nature of vaccines. He further suggests: "These experiments in tubes prove nothing more than an attenuation of virus by temperature, and cannot indeed be very happily compared with what happens to the animal organization under the influence of a hot climate. They explain some things but not all. Experimentation in the way of submitting animals to conditions that resemble the atmospheric phenomena, after having been inoculated with cords with the maximum of virulence, is the only way of resolving the problem." Dr. G. Ferris, in seeking the cause of death by rabies, was induced to try warming the animal, which in the paralytic stage becomes rapidly cold. This operation has

succeeded in prolonging life one, two, and sometimes three days. This has been done by placing the animal in a large oven, warmed and provided with a free circulation of air. The effect of natural high temperature on the rabic virus in the body of the hen (the temperature of which is 108° F.) is to render it sterile, inert, innocuous. The cloaca of the hen might be used for minor experimental purposes as a thermostat set at 108° F. The effect of artificial external heat on the rabic virus in the body will be considered in the section on therapeutics. Rabic virus retains its virulence intact for several weeks in the encephalon and cord if the cadavers were preserved from putrefaction by keeping them at a temperature ranging from 0° to 12° C. (2° to 53° or 60° F.). The virus, enclosed pure in glass tubes sealed by the blowpipe, can be preserved for three weeks or one month even at summer heat.

Dr. Byron suggested that a test tube be used with cotton soaked with glycerin and water at the bottom of which the cord rests; the open end of the tube is sealed by the blowpipe. Cords thus prepared can be safely transported. The following method I have used advantageously:

Take a sterilized test tube containing glycerin agar, flame the cotton plug and perforate it with a red-hot needle; then thrust the cotton down nearly to the agar (place the cord on top of the cotton), and seal with blowpipe the open end. The agar will exhibit growths should the material (cord) become contaminated. Fluid culture media can, of course, be used if the tube is not upset. The virulence of rabic material is best maintained at a temperature of about 23° C.

Suzor (1887) quotes from the communications of Pasteur as follows: The virus of an ordinary mad dog or of a mad rabbit injected directly into the veins of a dog generally gives rise to paralytic rabies. The same virus injected upon his brain produces furious rabies. Pure water, simple sterilized broth, or the same containing a quantity of pulverized marrow of 14 days' desiccation, the blood, the urine of a rabid animal, injected on the brain of a dog or rabbit, do not give rise to rabies. Such has been the result, at any rate, in a large number of experiments. There was only one exception in favor of the blood; and fourteenth-day marrow, if injected in very large quantities, does exceptionally reproduce the disease.

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The bodies and all the unused parts of dead rabid animals are put in a large tub, containing a 4 per cent. solution of sulphate of copper. Once a week the knacker comes around and carts them away. He plunges his bare arm in the liquid and deals with the carcasses just as if they were common non-rabid ones. Their virulence is all destroyed. Of all sterilizing agents it would seem that turpentine is the one that possesses the greatest activity in vitrio against the specific virus of hydrophobia. A glass rod, somewhat too hot, used in mashing and stirring up the medulla, may attenuate or destroy it. Neutral glycerin, unless tightly sealed, by reason of its hydroscopic property, may absorb acid and thus sterilize the virus (medulla) immersed in it. The virus of rabies, under proper precautions, is extremely persistent, and may be indefinitely propagated. It must, however, be classed as a virus of feeble resistance. Animal dead bodies and other virulent material may be sterilized by boiling, but cremation is altogether preferable.

Rabies is an infectious (contagious) neuropathy; neurosis is less cacophonic, but in usage this word has come to denote functional disease

of the nervous system. Toxineurosis is open to the same objection; these poisons almost always produce organic change.

INCUBATION.

The stage of incubation is of variable duration. "In 6 per cent. of all cases between three and 18 days, in 60 per cent. between 18 and 64 days, in 34 per cent. this stage exceeds 60 days. While this period is seldom less than 14 days, it is frequently protracted from three to six months. There is an authentic case of 18 months. But a duration of five, seven, ten and 12 years 'should be obviously regarded as mythical.' Fourteen days and five years have been given as extreme limits. Brouardel quotes the following statistics: 'Out of 170 cases rabies showed itself within the first three months; in another set of 97 cases it declared itself within the same period.' He concludes rabies supervenes oftenest in the course of the second month; rarely after the third month; quite exceptionally after the sixth month. The more numerous the bites and the greater their gravity the earlier do the symptoms appear. They manifest themselves earlier also in children than in old people." I have

known four children (boys), the eldest being 16 years, the youngest eight years, all bitten by the same dog at or about the same time, to develop rabies within thirty-five days, notwithstanding treatment. These children were bitten on the face and neck, and not efficiently cauterized (efficient cauterization in multiple and deep wounds is impossible). "The dangerous period for children bitten on the head and face rarely lasts beyond the fourth or sixth week." This assertion would be more in accord with strict fact if the nature of the bites was qualified as multiple and severe. Of course a mere scratch or puncture may cause the disease, especially if a nerve be involved; but such wounds can be more radically dealt with, and they are less apt than multiple and severe wounds to lacerate nerve and lymph structures. The foregoing relates to rabies in the human animal body.

In the dog the duration of incubation is "less than two months in 80 per cent. of the cases; very seldom longer than six months. Youatt gave one case of 11 months." The longest period of latency in the dog is fixed at eight months; the shortest at six to eight days. The disease occurs within two months in 83 per cent., within

three months in 16 per cent., four months and later in 1 per cent. In other domestic animals the period of incubation varies from two to five, seven, or ten weeks, and in exceptional cases may be extended to 9 or 15 months. During the stage of incubation the persons bitten (so far as observed, and minute observation in man is difficult of access) exhibit no symptom. They themselves have often forgotten the occasion of the bite. Slight wounds readily heal. Bites of rabid animals are imagined to have a peculiarly strong tendency to heal. Even after the application of strong caustics the wounds produced by the bites of rabid animals are said to manifest a strong tendency to skin over without granulating. Inflammatory reaction is generally slight and its pain moderate. Touching the scar is said to produce peculiar sensations—shuddering, feeling of anxiety, and sighing. It is necessary not to overrate the tingling, smarting, burning, drawing, and darting painful sensations common in cicatrices; atmospheric changes, rheumatism, neuralgia, may beset any cicatrix, and not rarely those produced by caustics.

These remarks are restricted to the stage of incubation. The early symptoms, the prodromes,

exhibit cicatricial signs more frequently in the lower animals, but they are present exceptionally in man. In animals there are experimentally observed in the period of incubation peculiarities of temperature and respiration; the former is easily recognized and of ominous portent. Dr. G. Ferri (1889) claims to have observed in inoculated rabbits a period of acceleration of respiration sometimes on the fourth day after inoculation, more frequently on the fifth. He advances the theory that this indicates the arrival of the poison in the floor of the fourth ventricle, which becomes virulent between the middle of the fourth day and the commencement of the fifth day. He does not think that elevation of temperature produces the acceleration of respiration. The temperature in 17 out of 47 animals rose after inoculation, 13 on the second day, three at the beginning of the third day, one at the end of the first day; then the temperature fell below the point of elevation some tenths of a degree. Feeble variations continued for five days, during which period for the greater part of the time it rose. It attained a maximum in the majority of cases on the sixth day, 14 times on the fifth day, 30 times on the sixth day, three

times on the seventh day. From the time of the highest elevation it began to descend and continued to do so until the death of the animal. The relative maximum on the second day is not constant; the absolute maximum occurring on the sixth day is constant. The relative maximum is only .74 of a degree; the absolute maximum is 1.5 degrees. This may be called the rabic rise of temperature. We have only seen it fail in one single case. If the accelerated respiration was caused by the elevation of temperature, the maximum of respiration ought to coincide with the maximum of temperature. Furthermore, the latter occurs on the sixth day while the former takes place on the fourth day. In some cases the abatement of the respiration has begun before the maximum elevation of temperature has been attained; consequently the respiratory acceleration does not appear to be dependent on the elevation of the temperature. In certain cases, however, it does appear as cause and effect, but in a general way one may say that the accelerated respiration occurs when the floor of the fourth ventricle becomes poisoned and is independent of the thermal phenomenon.

The saliva of the dog is virulent three to

eight days before any sign of rabies appears; the saliva of the rabbit at the time of the temperature rise, on the sixth day. Marochetti's eruption beneath the tongue, knots, vesicles, swollen orifices of the submaxillary glands observed by him, and by Drs. Magistel and Zanthos, may perhaps occur at times in various disorders, but are of no significance as indicating incubation of rabies. I know of no observations regarding temperature in human beings during this stage of rabies. As there are no symptoms, no investigation will probably be made at this period.

RABIES IN THE DOG.

There are two varieties of rabies. One is popularly recognized and feared as a dog run-mad. There is another in which the dog does not run; it is in fact paralyzed and cannot. It seeks retirement, hides away in obscure places, in fence corners, cellars, and under steps. Fortunately it does not tend to bite. In the early part of this condition biting is difficult; in the latter part it is impossible. The jaw is in a condition of paresis, and from the open mouth drivels a virulent saliva. Sympathy for animals is a com-

mendable trait; but in the case of sick or wounded animals it should be manifested with discreet caution. A little dog run over by the street cars was picked up by a gentleman, who was bitten by it on the hand. From this wound rabies developed. A stray cur taken in by some children was fed by their father, who, in stooping to do so, was bitten on the ear and died of rabies.

The typical mad dog exhibits three stages. In the first the dog is dull, depressed, fidgety, nervous, restless. In the second it is delirious, maniacal, furious. In the third stage it is imbecile, helpless, paralyzed. In the beginning of rabies there is an alteration in its usual behavior and disposition. In its conduct it evinces a variable disposition to those around it, being either more confiding and friendly than usual, or the opposite, irritable, morose, and easily enraged. An undemonstrative cross dog becomes friendly or even caressingly affectionate. An amiable dog becomes snappy and cross. There is a peculiar condition of hyperæsthesia at times; it crouches away from the touch and is easily frightened. There is moderate conjunctivitis, the eyes are red, sad looking, and distrustful. Its attitude indicates suspicion and sickness. The

appetite is disordered. It refuses food, except some choice bits, and the food is apt to escape from its mouth; it drops it. On the other hand it swallows all sorts of unfit things—hair, straw, dung, rags, earth, stones, bits of leather, and wood. It licks cold objects eagerly—stones, iron, the noses of other dogs, and its own urine. At times the sexual instinct appears to be excited, constantly smelling and licking the genitals of other dogs. It is shy, uneasy, springs at the door, has spectral illusions, and obeys reluctantly. Its movements show signs of uncertainty, incoördination; there is weakness and tremulousness of the hind part of the body. It wanders about the house and yard, seemingly seeking a remedy for its discomfort. It may still obey its master, and in most cases spares those to whom it is attached; but if persistently disciplined it may lose its self-control and bite. It may lick and gnaw its wounds and cause them to become inflamed. Sometimes there is excessive itching. The eye is frequently closed for several seconds; there is defluxion from the nares, a tendency to choke, difficulty in swallowing, and a disposition to vomit. The voice—and this is an important sign—even at this early period, is altered, hoarse,

muffled in the bark, which is rather infrequent and difficult to evoke. It is, according to Bouley, quite peculiar, and once heard is not forgotten. " Instead of bursting out with its usual sonorousness and being made up of a succession of notes equal in duration and in intensity, it is hoarse, veiled, lower in tone, and after a first full-mouthed bark there follows immediately a succession of five, six, or eight howls coming far back from the throat, and during which the jaws are never completely closed, as they are ordinarily after each bark. It is not unlike the voice of a dog chasing a hare; it is something intermediate between a bark and a howl made up of the two with something added, stronger and sinister " (Suzor).

In some cases the dog is voiceless. As a rule the stages gradually pass into one another. Sometimes there is a sudden outburst. The symptoms of this first stage may be very insignificant; nor are they uniformly present. And for this reason the greatest risk is incurred by man at this stage. Many of these symptoms are of short duration and, moreover, are present in other diseases; therefore their diagnostic import is slight. The bark is perhaps peculiar,

and is due rather to paresis of muscles of cheeks, mouth, and jaw; the voice is laryngeal. The tendency to fall, the fore legs giving way under it, is also a noticeable paresis. The dull, voiceless dog crouches in dark and quiet, trying to sleep, which is broken by dreams, hallucinations, and delusions, which also characterize its waking hours. "Seeking rest and finding none," it gets up and walks about. In some cases there is an absence of this restless agitation; it is sleepy and pays no attention to what is going on around. If disturbed it growls, but shows no inclination to stir. This condition may usher in the paralytic variety, but it occasionally, and for a time, is present in the typical rabies. There seems to be a displacement of special symptoms, and indications exist of that which subsequently becomes very pronounced. The slight paralysis, paresis of the first stage, indicates the complete condition of the third; transient outbreaks of violence presage the furor of the second stage. Slight alteration of voice precedes its marked change, and final extinction; excitability increases. In a room the dog runs about persistently, noses under the furniture, tears the curtains and carpets, bounds at the wall, jumps

and snaps as though catching flies. It sees things which are not, and hears sounds that have no outward source. All this, says Youatt, may be dispelled by its master's voice. The dreadful objects vanish and it creeps to its master with the expression of its peculiar attachment. Now follows an interval of calm. It slowly closes its eyes. Its fore legs give way and it seems about to drop. Suddenly it gets up again. Fresh phantoms rise before it. It looks about with a savage expression and rushes as far as its chain allows against an imaginary enemy.

It is thirsty, laps fluid eagerly but cannot swallow it; but in some cases it can swallow solids, and this it does without discrimination, so that foreign and unusual substances in a dog's stomach arouse suspicion of rabies. It bites and tears rough substances, lacerating its mouth so that blood in the trachea, œsophagus, and stomach is not unusual. At first for a short time the appetite may be increased, but soon it is lost. But it may eat or at least swallow, gulp down food and other things within reach. The popular idea is apt to be rash and sweeping in generalization. If a dog can and does eat it cannot be mad, may be a rule, but it has exceptions. A

patient assured me that a dog which bit him ate "naturally all the time." I know that it swallowed meat put in its box; because I saw the meat put in, and after observing it all the time I had it shot and found no meat in the box. It took the muzzle of the pistol, which had been thrust through a knot, between its teeth; the discharge tore its medulla oblongata to pieces. Previous to the discharge it was violently active, rushing from side to side and tearing the wood of its box. Afterwards, instantly there was a cessation of everything, not the slightest sound or movement. The death was as quick as the pistol shot. The dog at times will respect its master and recognize his voice, but not always at all times. A gentleman recounts the circumstances under which he was bitten: My dog had abandoned its home, but returned. I called it; it then rushed upon and bit me. If I had not thus attracted its attention I do not think I should have been bitten. Another idea with an element of truth is that a mad dog usually runs straight, will not deviate from its course. This it may do when amaurotic, almost blind, pupils widely dilated, weak, and tottering. It may have no inclination to go aside. But when it

will and when it will not is a factor impossible to determine practically.

The foregoing is a composite picture of the first stage of furious rabies. Very rarely does the one case present all the features, and very rarely also some one case may present none of them. "The animal remains tame and unaggressive to the end, but as a rule in the second stage it is in a state of delirious rage, about which there can be no mistake as to its significance. If chained in a cage it bites and tears at everything thrown at it. It attacks furiously all animals that come within its reach, later on man also, and more rarely its own master." It seems to have lost the sense of pain or the expression of it. It breaks out its teeth and tears its body. If now it can break away, and it makes strenuous efforts to do so, it runs amuck biting many other animals over a long district, and some of these in their turn developing rabies propagate it endemically. It is no unusual experience in institutions treating rabies to have several patients from about the same district bitten at distant intervals of time. The advice to kill all animals bitten is sound, but in rural districts it is impossible to know all the animals that have

been bitten. The familiar picture of the tail drooping between the legs, the open mouth, the dripping saliva, the sideways gait, the stagger, is that of the beginning of the end of the third stage. Before further adverting to this stage it is important to note that a mad dog, fighting and biting furiously, *rarely or never barks,* which other dogs in fighting do incessantly.

Viewed from a distance the wandering mad dog presents no peculiarity of gait; its tail is held high and wagging, there is no dribbling of foam so long as it can swallow. "Its course is sometimes straight forward, sometimes in diverse directions or in circles."

No especial dread of water is manifest, nor is there aversion to air, light, or, except in rare instances, to the glare of the sun. The fæcal and urinary excretion is scanty. Eating but little there is not usually bowel obstruction. Occasionally the large gut is filled with dirt and hair. Emaciation is rapid, caused by excessive waste and excretion, the eyes become sunken, the coat rough, and the body thin. The mucous membrane of the mouth is but slightly moistened and is often parched and of a dirty, livid color. A discharge of saliva and foam from the mouth

is scarcely ever seen. The respiration may be hurried, but is usually but slightly affected. The pulse is slightly accelerated and often irregular. The third, the paralytic stage, develops directly from the previous stage, the paroxysms becoming weaker and less distinctly separated from the remissions. The maniacal rabid dog, like the human maniac, after longer or shorter duration of furor has longer or shorter periods of exhausted quiescence. Increasing exhaustion, increasing paralysis, especially of the hind legs, ensue. The gait becomes uncertain and staggering; the dog can scarcely stand and trembles from side to side. Often it lies curled up as if attempting to sleep, raising itself on its fore legs only when irritated. It may still attempt to bite or at least snap; the voice is hoarse, there is dyspnœa, and small, thready pulse. At times partial or complete convulsions occur. Death usually takes place on the fifth or sixth day; rarely prolonged to the seventh or eighth, and never beyond the tenth day.

Paralytic rabies, dumb madness, sullen rabies. Inoculation experiments from this form of the disease often reproduce the disease in its furious form and *vice versa,* showing that the two forms

are only varieties, though very different, of the same disease. This form of rabies exhibits itself in about 15 or 20 per cent. of all cases. Formerly this form was supposed to be the first stage of the disease, and the rabid form the second stage. Now it is regarded as the immediate passage of the first stage into the third stage, the second stage having been omitted. Experimentally in young dogs the disease may begin and end suddenly and abruptly in the second stage.

June 14th, 1897, 1 p. m.: Bitch trephined and inoculated subdurally from medulla oblongata of a rabbit dead of rabies from subdural inoculation of a fixed virus; 120 removes.

June 23d, 1897, 8 a. m., at which hour the previous evening there was no grossly apparent disease. It is now running about the cage, biting at its sides and at the vessels in the cage, butting its head against the cage. Its bark is hoarse, howling, squeaking. It had three tetanic convulsions and died at 10 a. m. same day.

Post-mortem Examination.—Integument of scalp contused by butting cage. Lungs ooze serum freely; kidneys hyperæmic; bladder empty; stomach contains sawdust and hair.

January 15th, 1898, 2.30 p. m.: Black and tan cur, young, not fully grown; weight, 10 pounds. Trephined and subdurally injected with emulsion, in sterilized water, of medulla oblongata of rabbit which died of rabies from subdural inoculation of fixed virus; 138 removes. Anæsthetic administered during operation—10 grains of sulphate of morphine hypodermically.

January 23d, 4 p. m.: The dog was at this time gentle and answered when called, jumping up on sides of cage. Without doubt the saliva was at this time virulent. Had this dog bitten some one and passed from under observation, and the bitten individual subsequently died of rabies, a biased mind would see a case of rabies from bite of dog that had it *not*. A fact relative to alteration of voice is noteworthy. The hoarse tone of voice, the peculiar laryngeal vocalization may disappear at irregular intervals and return. I have observed this in a human being with rabies. Though generally his utterance was laryngeal, for a few moments, a few sentences were uttered distinctly, showing that at this time the nerve disorder was one of incoördination, paresis rather than complete paralysis.

January, 24th, 1898, 7.30 a. m.: Biting basin

and growling. 8.30 a. m.: Barking, apparently naturally. Biting sides of cage, jumping and falling about. Broke its teeth, seized its hind leg between its teeth, held it, chewing on it and biting it. 1 p. m.: Same dog exhausted, and now made no attempt to bite a bitch put in cage with it. Just before death it barked, apparently naturally; convulsed, it died at 1.30 p. m.

The medulla oblongata of this dog was inoculated subdurally into a small, young black and tan cur, weighing 9 pounds. This was done on January 24th, 1898. February 1st this dog suddenly developed furious rabies. The evening before it was gentle and timid. It furiously attacked a dog put in the cage with it, fighting and all the while not barking. The bitten dog has not at this date, June 9th, 1898, shown any sign of rabies. The rabid dog was observed to have the disease about 7 a. m., and died at noon on same day, exhausted. When fighting with the other dog it would become exhausted and lie down panting, and after a time get up and renew the attack. These cases strikingly contrast with that of an immense, previously ferocious bulldog; which being experimentally

rabid could not be forced to bite another dog, and Pasteur was compelled to take the saliva from its mouth. He remarks that it is well known that a bitten dog, if it takes the disease, shows in the majority of cases furious rabies with a propensity to bite, and possesses the special rabid voice.

In the habitual run of our experiments, when we inoculate the rabic virus into a vein or the subcutaneous cellular tissue, we more often give rise to the dumb or paralytic form of rabies, voiceless and tame. By intracranial inoculation, on the other hand, the rule is that furious madness is produced. We have also ascertained that it is possible to give rise to furious madness by intravenous or subcutaneous inoculation, provided that very small quantities only of the virus be used. The smaller the quantity of virus or diseased material used in the entire venous or hypodermic inoculation the more certainly is the furious form of rabies reproduced. By the inoculation of small quantities of virus the duration of incubation was increased, and the same virus, if diluted beyond a certain limit, which is not very far, remains without effect when inoculated. Let it be carefully noted that a fixed

virus inoculated in very small quantities may produce a very prolonged stage of incubation in the first passage, but a second passage, with the usual quantity, exhibits the incubative period of a fixed virus.

In paralytic rabies the disease runs a shorter course. The symptoms of cerebral irritation are slight in degree, the animals are less lively and active, appearing silent, quiet, and depressed (even in human beings with this form of rabies, silent gloom and unnatural passivity, morbid inactivity, are marked characteristics). Excitement, the propensity to stray or to bite is less frequent. There is no aversion for fluids. The voice is a howl with no admixture of bark, and soon is lost altogether. The mouth is constantly open, owing to paralysis of the lower jaw; the eyes without expression and constantly fixed in the same direction. The predominant symptoms are muscular weakness and cerebral depression. The animal is constantly lying down or sleepy; it has neither the will nor the power to bite. Everything taken into the mouth falls out again. There is the genuine frothing saliva and mucus flowing from the open mouth. Absence of defecation, and of appetite. Rapid emaciation and

death much more quickly than in the furious variety, taking place within two or three days. The great majority of cases of canine rabies end fatally; a few exceptional cases are, however, on record in which the disease spontaneously or under the influence of medicine gradually disappeared. Submersion in cold water until asphyxia is nearly complete; the so-called sailors' cure; the bakers' hot-oven cure; the excision of the sublingual vesicles, calomel, bleeding, enemata, broom top, or almost any other old thing, is unworthy of scientific credence. The requirements for getting "on record" used to be not very strict. The time is past when the medical mind can be occupied with garrulous relation of "remarkable cases," utterly without careful experimentation. Sometimes these cases are bolstered up with ill-concocted attempts at demonstration, illustrating nothing except the psychological tendency of the human animal to monkey with things, an evolutional argument overlooked by Darwin. That dogs and other animals have recovered after the manifestation of the very early symptoms there can be no doubt, and may thereby acquire immunity. That in man, under similar circumstances, the same might take

place is a possible occurrence of which there has been no rigorous scientific demonstration.

RABIES IN THE RABBIT.

The signs and symptoms of this disease in the rabbit are interesting in themselves, and additionally so because this animal is usually selected for the demonstration and production of rabies, and its spinal cord used in the prophylaxis. The rabbit is inoculated by trephining and subdural injection of rabic medulla oblongata rubbed up in bouillon or sterilized water. A piece of medulla from the floor of the fourth ventricle, of about 4 c.mm., is rubbed up in about 10 c.c. of sterilized menstruum, and of this 3 or 4 minims are injected beneath the dura mater, or small pieces (about 1 c.mm.) may be introduced through small slits in the dura and gently pressed against the brain and withdrawn, or they may be allowed to remain. If the virus be not fixed, if it be from some animal ordinarily rabid, the first signs of the disease manifest themselves between the twelfth and twentieth day, usually on the fifteenth day. With the fixed virus the first manifest sign takes place on the seventh day, that is, after six days. This sign is elicited by

pushing the rabbit. A sudden, quick push sideways, alongside the thorax, causes the rabbit, in regaining its equilibrium, to sway, oscillate from side to side; especially is this observable in the head and neck. The eyes are unusually glistening and the ears often held erect. In some cases there is marked gritting of the teeth and continuous chewing movement of the lips. The incoördination just referred to rapidly increases; in 12 hours the rabbit falls sideways if caused to run, or tumbles on to its back, kicking and struggling ineffectually to get on its feet. There is often a grotesque pose, the head is thrown backwards or to one or other side and shaken; the limbs are projected before or behind or sprawled out laterally; the body may be curved sideways or bent backwards in marked opisthotonos, in which position after death it becomes fixed. This incoördination eventuates in complete paralysis, the rabbit lying helpless on its side. But in this first stage there is no ordinary paralysis; the animal held up by the skin of the back kicks vigorously. There may be slight convulsions, or the tremor always present may amount to convulsive movement or the convulsion may be very violent. But with all this muscular exertion the low tem-

perature of this stage is maintained; the thermometer introduced its entire length up the rectum indicates no rise of temperature. Generally the incoördinate stage is very marked; sometimes it is very slightly if at all present in these cases; the paralytic element predominates from the first. The animal is loath to move, is stiff, and drags itself along with difficulty. The whole body is depressed downwards, the belly too close to the ground. The muscles of the scapula and pelvis seem paralyzed and allow the body to settle downwards. The animal tends to be more quiet in this form than in the first.

Furious rabies cannot be predicated of the rabbit, but it has its semblance in an excited form. Occasionally the rabbit does not exhibit the usual incoördination or the rarer paralytic form. Let out of its cage into the room it runs about excitedly. After running for a time forwards, it runs backwards several steps; it stops still and jumps upwards, thrusts its head in a corner and paws at the floor; and this pawing it repeats energetically if disturbed. If a stick be pushed at its mouth it makes some forward movement of its head as though about to bite, but it is doubtful. A rabbit can perhaps be taught to

bite a person, but it is not its natural inclination. I have known an employee to be bitten because he, placing his hand beneath the rabbit's mouth, moved it (his hand) from side to side on the floor of the box, spreading the sawdust; this manœuvre is a risky one. The finger was somewhat badly cut, and the attendant was treated because the rabbit developed rabies in 24 hours after the bite. In the excited form paralysis ensues, but it comes on late as a last stage; the incoördinate stage has been replaced by the excited stage. This stage of incoördination, so emphasized in the rabbit, finds expression in other animals in their tendency to fall down. Their legs give way under them. The rabbit not infrequently tears open the operative wound, paws it apart, because of some disagreeable sensation. There is a mucopurulent discharge from the conjunctiva. The cornea sometimes becomes opaque. The stools are pultaceous; not balled as normally. Before the onset of the nervous symptoms there is a rise of temperature, irregularly coming and going when the disease is a result of unfixed virus. With the fixed virus the temperature elevation immediately precedes the nervous symptoms. It soon falls and continues to drop until death.

The domestic tame rabbit is used for experimental purposes; the wild rabbit cannot be handled and dies in captivity, injuring itself by violent impact with the cage. The wild rabbit bites persons when it is well, and would also do so if sick with rabies. Why the domestic rabbit with rabies does not bite man it is not easy to explain. To say that biting is not a natural mode of offence and defence with a tame rabbit is to mistake a fact. The buck (male) rabbits are very fierce fighters, biting like dogs each other's bodies and tearing with their teeth each other's ears. They also bite and tear out the testicles.

[The following is a detailed report of the first rabbit (first remove from cow and second remove from dog) inoculated with rabic medulla oblongata. This is the first rabbit of the series that has now reached 155 removes, June 10th, 1898.[1]

October 5th, 1893, 4 p. m.: Rabbit X′, weight 2 pounds, was trephined without anæsthetic and pieces of medulla oblongata of cow No. 1, bitten by dog No. 15, were introduced beneath dura.

[1] July 17, 1909, 500 removes.

Temperature of room, 20° C.; temperature of rabbit before trephining, 102.8°F.; immediately after, 101.2°.

	Temp. of Room.	Temp. of Rabbit.
October 6th, 3 p. m.	20.5°C.	103.6°F.
October 7th, 3 p. m.	20.5	103
October 8th, 4.30 p. m.	22.5	103.8
October 9th, 2 p. m.	22.5	104
October 10th, 5.15 p. m.	23.5	104.4

After food and exercise which elevate temperature.

	Temp. of Room.	Temp. of Rabbit.
October 12th, 2 p. m.	20°C.	103.6°F.
October 13th, 3 p. m.	20	103.6
October 14th, 5 p. m.	24	104.2
October 15th, 3 p. m.	17.5	105

Eleventh day, rabic rise of temperature. Seems well. Paws the wound on head, which is well healed. Another rabbit licks the wound and nibbles off the hair. Weight, 1 pound 13½ ounces; lost 2½ ounces in weight.

	Temp. of Room.	Temp. of Rabbit.
October 16th, 1893, 4.30 p. m.	17°C.	104°F.
October 17th, 4.30 p. m.	16	103.4
October 18th, 6.30 p. m.	19	103
October 19th, 5.30 p. m.	19	102.8
October 20th, 5 p. m.	20	101.8

This is the sixteenth day and exhibits the rabic temperature drop.

October 21st, 6 p. m.: Temperature of room, 21.5° C.; temperature of rabbit, 102.2°. Temperature fluctuation; rabbit lively.

October 22d, 2.50 p. m.: Temperature of room, 20° C.; temperature of rabbit, 101°. This is the eighteenth day; rabbit is thin but active and playful, and eats moderately.

October 23d, 5.40 p. m.: Temperature of room, 22° C.; temperature of rabbit, 100.4°. The rabbit droops at times, sits around with its ears along its back; is getting thin progressively and has low temperature (abnormal). At other times it is active, lively (excited?), playful, and somewhat vicious, snaps when annoyed, and strikes with fore feet. Voids soft stools.

October 24th, 1893, 6 p. m.: Temperature of room, 23° C.; temperature of rabbit, 100.4° F.

October 25th, 1893, 2 p. m.: Very sick. Jumps around but is very weak, falls over; hind legs are certainly not markedly paralyzed, and it is difficult to determine whether, when animal attempts to jump, it falls over from weakness (paresis?) or incoördination. Ears cold; temperature of rabbit, 93.4° F. Died at 5 p. m. This is the twenty-first day. Weight, 1 pound 3 ounces. Weighing before inoculation 32 ounces, it has lost 13 ounces.

Rabbit O′, trephined and injected subdurally

with emulsion of medulla oblongata of rabbit X′, developed rabies on thirteenth day. Rabbit F′, trephined and injected subdurally with emulsion of medulla oblongata of O′, developed rabies on thirteenth day. In both these cases the very large amount of 1 c.c. of the emulsion was injected. Post-mortem examination of rabbit X′: *excited* rabies.

Brain seems normal (grossly); no gross lesion at site of trephining. Medulla oblongata grossly appears normal. Lungs pink, collapsed. Heart blood coagulated. Stomach moderately filled. Liver grossly normal. Spleen very small; weight, .2 gm. Kidneys grossly normal. Bladder full. Cæcum full of pultaceous fæces; this gut is very rarely observed to be empty—even when a rabbit has been for some time deprived of food this bowel is full of pultaceous fæces.]

Excited rabies, according to Pasteur, is more apt to supervene in first passages—that is, from one species to another, analogous to serum poisoning, but it is not absolutely absent in inoculation with fixed virus. Pasteur thinks that an animal is more apt to escape when a very large amount of emulsion is injected than when the dose is the usual medium amount, 5 minims;

he supposes that a large amount of antitoxin is also injected. Suzor gives the following experiment: One-half cubic centimetre of emulsion of rabic medulla is injected into popliteal vein of a dog. On the tenth day this dog begins to lose its appetite; on the eighteenth day it is completely paralyzed, and dies on the twentieth day, without having at any time the peculiar bark of a mad dog, and without any attempt to bite. To a second dog $\frac{1}{100}$ part of $\frac{1}{2}$ c.c. of emulsion is given intravenously. On the thirty-eighth day it looks suspicious; on the thirty-ninth day it has the rabid voice, and dies on the fortieth day. A third dog intravenously injected with the $\frac{1}{200}$ part of $\frac{1}{2}$ c.c. takes no disease at all. Rabbits inoculated should be kept under observation at least 90 days, because it is known that rabies may develop after such interval of time. Dr. Wesbrook (University of Minnesota) has informed me of an interesting series of this nature.

[The above is a very small dose of fixed virus, the second passage with usual dose will exhibit the usual period of incubation (six days).

The following are the details of rabbit O′, trephined and inoculated from rabbit X′:

October 25th, 1893, 5.30 p. m.: Rabbit O′

trephined and injected with 1 c.c. of an emulsion of medulla oblongata of X′ in bouillon. Temperature of rabbit, 104.2° F.

	Temp. of Room.	Temp. of Rabbit.
October 26th, 5.45 p. m.....	18°C.	104.4°F.
October 27th, 4 p. m.	18	103.4
October 28th, 5.30 p. m.....	19	103.8
October 29th, 4.45 p. m.....	14.5	103.8

After food and exercise.

	Temp. of Room.	Temp. of Rabbit.
October 30th, 5.45 p. m	——	103.6°F.
October 31st, 6.15 p. m.....	16.5°C.	103.2
November 1st, 4.45 p. m.....	18	103.2
November 2d, 6.15 p. m.....	19	103.2
November 3d, 4.50 p. m.....	18	103.8
November 4th, 4.40 p. m.....	17	105.4*
November 5th, 4.10 p. m.....	16	104.2
November 6th, 3.30 p. m.....	18	102.2†

* Eleventh day, rabic temperature rise.
† Thirteenth day, rabic temperature drop.

Indisposed to exertion, allows itself to be easily taken. Respiration hurried.

November 7th, 3.45 p. m.: Temperature of room, 19° C.; temperature of rabbit, 100.8° F. Fourteenth day, very marked tremor. Intestines observed moving beneath skin. Ears vertically erected. Constant movement of nose and upper lip. Stretches its hind legs out in extension; back depressed concavely; runs about excitedly; eyes preternaturally glistening; in running hind legs are at times jerked from under it and it falls

on one side of buttock. At other times it lies quietly on its belly, hind limbs extended, and head resting on one side, until disturbed by the advent of tremor.

November 8th, 1893, 4.15 p. m.: Temperature of room, 19° C.; temperature of rabbit, 99.2° F. Fifteenth day: Sometimes it moves round in a circle because it uses only its fore limbs; at other times it runs forward, but falls over from incoördination of hind limbs; hind legs sometimes outstretched backwards and head retracted; hind legs often give way under it.

November 9th, 4 p. m.: Temperature of room, 19° C.; temperature of rabbit, 101° F. Sixteenth day: Lies with head much retracted, struggles convulsively, and attempts to rise, but legs are useless. There are convulsive movements rather than pronounced convulsions. At times hind legs are extended tetanically with a thermometer that can be introduced only 1½ inches; temperature is only 84° F., with thermometer graduated to 90° F., introduced all its length. No temperature is registered November 9th, 6 p. m.

November 10th, 8 a. m.: Seventeenth day found dead and put on ice.

November 10th, 3 p. m.: Post-mortem examination: weight, 2 pounds 18 ounces; rigor mortis marked.

Brain—very vascular, pial hyperæmia; site of trephined area; dura mater, opaque white, thickened, amber-color fluid effused beneath. Medulla oblongata—membranes very vascular. Lungs—bright red. Spleen—weight, 4 gm.; length, 3 cm.; width, 5 mm.; thickness, 2 mm. Bladder—very full, paralysis of. Two pigeons were trephined from this rabbit, but failed to develop rabies. Pigeons are difficult to inoculate successfully with rabies. They, however, bear the trephining very well.

These two cases, rabbit X′ and rabbit O′, exhibit two different forms of rabies, X′ being excited and developing paralysis late, nineteenth day, and dying on twenty-first day. O′ developed rabies on the fourteenth day (incoördinate form) and was found dead on the seventeenth day. The post-mortem appearances also differ. In X′ the brain is normal. In O′ the brain is very vascular, dura thickened at site of trephining. In X′ the lungs are pale, collapsed. In O′ the lungs are bright red. In X′ the medulla oblongata is normal. In O′ the membranes over medulla oblongata are very vascular.]

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UNIVERSITY OF LEEDS

RABIES IN THE HORSE.

As usually observed in the horse rabies is of a violent character; not that the quieter forms do not exist in this animal, but they escape observation and are ascribed to other causes. The horse, at the beginning of the attack, is excited and subject to illusions. Excessive fright speedily ensues with tendency to bite, neighing and gnashing of teeth, sexual excitement, and loss of appetite. The specific paroxysms are very severe; the animal begins to kick, strike, and bite the objects about it, or held towards it. It often wounds itself, tearing off with its teeth portions of flesh of the fore legs and flanks. It will also seize other animals. It rubs the nose and mouth and makes peculiar motions with them. Respiration is accelerated. Weakness and paralysis of the hind parts take place. Death generally results in four or six days.

A mare, weight 1100 pounds, aged 20 years, was bitten by a supposed rabid dog October 11th, 1893, was taken sick November 1st, 1893, and died November 2d, 1893, 2 p. m. Dr. Tatum, veterinary surgeon, states that the mare was stiff and would fall down. Had tonic and

clonic convulsions with head retracted. Saliva running from mouth. Bit the stall and a man. Could not eat, could not swallow. Fæces and urine involuntarily passed. Post-mortem examination: Rupture of seratus magnus and diaphragm, supposed from spasm. Medulla oblongata seems softened, and there are numerous small hemorrhages into its substance. The dog that bit this horse had changed voice, snapped at chairs and bushes, and could not drink. Tongue black and " drawn up to a chip " in its mouth. From the medulla oblongata of this horse rabbits were trephined and inoculated subdurally; 60 rabbits developed rabies from this medulla, which has been before referred to.

The following article from the correspondence of the *Commercial News,* headed " A Mad Horse on South River," is copied because it graphically describes the disease, April 17th, 1894. " Mr. Scott Mackey's dog has gone mad and bitten a horse and cow. The horse has since gone mad; went mad just four weeks from the time she was bitten. While hauling fodder it was noticed that the horse was very irritable, and in other ways acted rather strangely. After dinner Mr. Mackey saw that she had eaten none

of her food, and for fear she was going mad he placed her in an empty pen of his hay barn. The next morning a man looked through a crack of the barn at her, and with her mouth open she plunged towards him. Her colt was lying between her and the crack and she caught it by the top of the neck. All day she was pawing, neighing, and shivering as with cold (tremor?); would suddenly fall, then with great effort get up again and plunge at every one. In the evening she became more violent; she suddenly dropped to the ground as before, and seizing her front leg between her teeth, began to crush the bone and tear the flesh from it. She then got up, the blood streaming from her wounded leg. Again she fell and began chewing her leg, whereupon she was shot. We have partly seen the damage done by this dog; but what is to come may be more terrible, as the dog left home Saturday evening, ran over the South River country all Saturday night, Sunday, and Sunday night. It came home Monday morning, apparently in fine humor; was at home all day Monday and no one suspected it rabid until after it bit the horse and cow late Monday evening. Mr. Mackey then got a biscuit and called the dog to

him. The dog followed him to the spring house, where it was fastened up. Next day it was paralayzed and unable to get up and was killed."

In this case a man calls his mad dog and it follows him obediently; in the case previously referred to a man calls his mad dog and the dog rushes at him and bites him. Rules and regulations relating to rabies abound in exceptions.

RABIES IN THE BOVINE SPECIES.

In cattle the symptoms are sometimes like those of the horse. They bellow often and loud in a hollow sounding voice, show signs of mental derangement, stamp and butt so violently as to break off their horns. They seldom bite. Paralysis occurs and they die after from four to seven days.

The following is the history of the cow from the medulla oblongata of which the series of rabic subdural inoculations were begun, October 5th, 1893, with rabbit X′ (previously referred to), and continued to date, June 10th, 1898, being now over 150 removes.[1]

This cow was reported to have been bitten on its nose July 23d, 1893. On September 28th she carried her head up and her eyes had a wild

[1] July 17, 1909, 500 removes.

stare. September 29th: She stopped eating and drinking and followed another cow around all day. September 30th: She could not eat, drink, or swallow her own saliva; what she did not blow out when bellowing dribbled from her mouth. Bellowing almost constantly; voice not unusual. October 1st: Bellowing somewhat like the voice of an ass; cannot eat or drink; looked wild out of the eyes; seat of bite red and congested. October 2d: Sore opened up and very red; voice better. In the evening drank about 1 quart of water; was brighter but would at times drop as if struck with an axe on the head (this is a peculiar sign); is now eating a little. October 3d: Drank a bucketful of water; ate corn, apples, hay, cabbage; redness all gone and sore closing. Throat swelled from ear to ear; she could not get her head down; voice of pharyngitis. October 4th: Respiration difficult, incessant bellowing; could not eat or drink. Throughout attack would fall if an attempt was made to milk her; no evidence of viciousness, no paralysis, no spasm. Three other cows had like symptoms. Died October 5th. Post-mortem examination: Body warm internally. Very little rigor mortis. Ulceration (?) of pharynx,

larynx, and trachea. Ulcers have an irregular contour and a yellowish-white membranous deposit. Dirt and a nail, which had punctured, were in the third stomach.

It is very doubtful if this cow would have been regarded as rabid from the signs and symptoms. The only sure diagnosis is demonstrative, experimental inoculation. The case just related is in many respects atypical. The case about to be reported is in most respects typical of furious rabies. Both of these cases were attended by William R. Tatum, D. V. S., who says: "I was called to see the cow because she was reported to be in labor and making no progress, and furious with the pains. She was bellowing almost constantly in a peculiar manner. I found the cow charging on a straw stack, as with intent to heave it down. She had gone through two fences to get at it. It was about seven hours since they had noticed anything wrong; she had been growing worse all the time. She was a young cow and I saw no sign of parturition; asked why they so thought, they said, Wait and you will see the calf's head. I had not long to wait before a pain came on, shaking her slightly from the head to the hind extremities (tremor?),

then followed spasmodic contractions of the abdominal muscles, especially the recti. At this the rectum opened and air rushed in; at the same instant there was a prolapse of the vagina with the os uteri in the centre, which they mistook for the calf's mouth and nose. The os was firmly closed; there had been no escape of liquor. This lasted a second, only to be repeated in quick succession, or after an interval of several minutes. Cow was bellowing constantly when not charging at something. The bellowing had a jerking rattle, I think due to saliva in the pharynx and larynx, which ran from the mouth and could not be swallowed, although frequent attempts were made, producing a sound more like the bray of an ass than that of a cow. On approaching her she made toward me, and I halloed at her, when she dropped to the ground as if struck in the head. I was at once struck at the similarity of this fall and the fall of the cow and horse whose brains you so kindly tested, and she like them at once got up again almost as quickly. This fall is more of a sudden dropping straight down and backwards, landing the body a little back from where it was, more than anything else that I can describe. We removed her

to a pen and gave her a bucket of water. She made a number of attempts to drink and was apparently drinking, but none left the bucket. Soon she began to fall and get up again and try to drink; and every time she would try to drink she would fall. After doing this a few times she got up and charged on the bucket, running one horn through the bottom, and became very much excited, fell down, and had a short tonic spasm followed by a clonic one in which the vagina was prolapsed more than at any previous time. I asked her owner to bring his dog down; the dog was no sooner seen than she dropped and immediately regained her feet and started for it, and came against the enclosure with such force as to break the rails. I tried her on some corn which she ate with great difficulty, until some chickens ran in to get their share of it, when she became again furious, charging at them and falling. The owner said that a dog had bitten a number of his cows and that a heifer was sick and would fall like this cow; but at no time was she violent, and drank milk up to the day of her death. The cow was shot. I did not make a post-mortem because my hands had fresh sores on them. I opened her mouth with two

sticks, and found part of the tongue and back part of throat bluish as though the blood had stagnated there."

Cattle die in from four to seven days. In sheep and goats the symptoms are like those of cattle; they make unnatural leaps, butt eagerly, soon become thin, and die paralyzed in from five to eight days.

Swine at first show fright; they hide away and become greatly excited by noises; they are wild and very dangerous. The disposition to bite is very great, and they tear first one ear and then the other. Respiration is accelerated. The visible mucous membranes assume a leaden hue, as does also the superficial integument. A viscid foam is discharged from the mouth and the eyes glisten. Death occurs in from two to four days.

Cats are timid and their symptoms difficult to observe. They are very uneasy, run about excitedly, and tend strongly to bite. Death results in from two to four days.

The domestic fowl when attacked with rabies manifests great uneasiness, springs about wildly. A hoarse voice is noticeable; also a certain tendency to bite and finally paralysis (Bollinger). Only the last two words are correct according

to my observation, and the following is from Suzor: Rabies in our hens never showed any violent symptoms, but only a degree of sleepiness, loss of appetite, paralysis of the legs, and frequently a considerable degree of anæmia or bloodlessness as shown by blanching of the comb.

A word of caution relative to experimentation. On one occasion I trephined a hen and injected subdurally some of the egg of a rabid hen. After a long incubation the hen became drowsy, gasped croakingly, and was pale in the comb. Most marked paralysis took place, and the case might have gone on record as inoculation of rabies from the egg had not the beak been opened and the membrane of diphtheria detected.

Wild animals lose their dread of man, whom they attack in remote settlements and outlying military posts. This applies to the wolf, fox, jackal, hyena, ferret, and skunk. Sometimes they make their way into villages, cities, and even houses. Many wild animals that die of quiet rabies and the paralytic form escape observation. The disposition to swallow unnatural substances is observed only in case of carnivorous animals. There is no aversion to water; they

lap it unless prevented by affections of the organs of swallowing.

The diagnosis of rabies is not to be excluded, because on post-mortem examination another disease is discovered. I examined a dog that had bitten a policeman. The right side of this dog's heart was full of balls of the long, slender worm called *Filaria immitis*. These worms filled the cavity and projected into the vessels. The stream of blood was, as it were, filtered through them, but there was no fibrin, no coagula. These worms were alive. Was their intact epithelium unfavorable to fibrinosis? The rabbits trephined from this dog developed rabies, and the man was treated. He is now well after several years.

RABIES IN MAN.

Rabies in man seems not to have been known until about 200 B. C. At this time in the writings of Celsus the word hydrophobia occurs. At a later date Plutarch, Pliny, and others describe the disease. Cœlius Aurelianus questions whether hydrophobia is a disease of the body or mind. Rabies was greatly feared by the ancients. They dreaded lest they should be bitten by those persons suffering with the disease, imagining that if

they came in contact with them the disease could be imparted. Even as late as 1840 those suspected of having rabies on the Austrian frontier were shot by their neighbors; and 50 years ago people were not unfrequently smothered when affected with rabies. " Rabies in man is an acute infectious disease, uniformly fatal, produced only by the implantation of a specific virus." In 90 per cent. this is the result of a bite of a rabid dog; cats, 4 per cent.; wolves, 4 per cent.; foxes, 2 per cent. These bites are seated in 53 per cent. on the upper extremities, 28 per cent. on the head and face, 22 per cent. on the feet, and 3 per cent. on the body or scrotum. To cause the disease it is necessary only to abrade the epidermis.

It has been stated before that the disease can be conveyed during its incubative stage in the dog. Every wound made by a stray dog that has escaped should be regarded as suspicious and treated accordingly. Accidental wounds producing rabies, as during post-mortem examination of rabid animals, have as yet only in one instance been satisfactorily proved. A student who had a small wound on his finger made an autopsy of a dog and died of rabies. This oc-

curred in 1857 at the Veterinary in Copenhagen (Bollinger). The period of incubation is uneventful; seldom it is less than 14 days; rarely, if ever, over 18 months. In the young it is shorter than in the old. After the expiration of the incubative period, which, it is asserted, may be shortened by excesses of various kinds, by cold, by hardship, by passion, the patient complains of loss of appetite and headache. He is in a state of depression and gloomy agitation. If questioned as to any bite he may have received he affirms that it is of no importance, and has nothing whatever to do with his malaise. He becomes ill-tempered, apprehensive, excitable. There is a mental disquietude by which he is driven about, without any definite object, or he makes a journey to relieve his nervousness by change of scene. He is often intensely anxious, contends against the idea that the bite is the cause of his uneasiness. In many cases he does not hesitate to deny that he has been bitten. He suffers with sleeplessness, and when sleeping has bad dreams. Many patients at this period are aware of the dangerous character of their disease, speaking frequently with a quick and sharp articulation of the coming serious ending. About

this time a not uncommon and a very significant symptom is an aversion to fluids. M. Trousseau relates that he was at one time called in great haste to a patient suffering from what was termed an indigestion of water. The patient complained of intense thirst and was firmly bent on drinking, but could not carry water to his lips without being seized with a deep feeling of terror. He could not take solid food either. This difficulty of swallowing after slight malaise in a man aged 37 years was a strange phenomenon. This sign marks the beginning of the second stage of rabies.

The Stage of Excitement.—The first stage is designated as the stage of melancholia, which may be very short. The patient is sad, silent, avoids company. There may be itching or pain at the seat of the bite, even though it is quite healed. This first stage seldom lasts more than four or five days. Sometimes there is a desire to walk or run in which there is mental irritability rather than melancholy. In the second stage the breathing becomes difficult, labored, sighing. The muscles receiving their nerves from the medulla oblongata become affected, producing spasmodic contraction of the pharynx and larynx.

Hyperæsthesia of all the senses may occur—dread of water, of bright objects, of draughts of air, odoriferous substances, and noise or sound. There are hallucinations of sight, hearing, and smell. The feeling of suffocation and the hallucinations cause the patient great anxiety and excitability. These paroxysms sometimes appear like maniacal attacks with delirium. They come on usually at the height of the disease, and the patient becomes furious at those about him, striking and insulting them. These symptoms are not usual nor do they last long. Afterwards the patient expresses great regret at his behavior. At times in this excited state he makes snapping motions with his jaws. The convulsions vary from the slightest to the most severe; they assume both the clonic and tonic form. On the second or third day the very characteristic sign known as sputation is present. The matter ejected is just ordinary saliva, and this the patient may spit in little pools about the floor or eject to some distance, even into the faces of the bystanders.

A man bitten in September, in January exhibited symptoms of rabies. A little girl and another man bitten on the same occasion devel-

oped no disease. Previous to January he had been unquiet, sad. He made a journey from home in search of recreation, when suddenly a few hours after eating a breakfast with good appetite he complains of very intense thirst, is seized with general shivering, loses his appetite, cannot swallow fluids, and is much agitated. This lasts for about 36 hours. General hyperæsthesia now takes place; he cannot wash his hands or face. Any attempt to do so brings on great agitation and violent shivering. This also occurs when he tries to comb his hair or beard. He dreads touching his person with his own hand. There are rare intervals of quiet. To the skin hyperæsthesia there is superadded a very acute and frequently repeated excitation of the genital organs, frequent erection, and seminal emission. Three days after the invasion of the disease his aspect creates alarm; he is agitated, garrulous, speaking in a curt, jerking manner. He cannot drink, although he is very thirsty, and when he attempts to doze he is immediately seized with clonic convulsions and spasms. The hyperæsthesia and satyriasis persist throughout the twenty-fourth day of January; the convulsive paroxysms become more frequent and he dies on the

fourth day, without having manifested any mental disorder or any hallucination of sight or hearing.

The above case illustrates many of the symptoms of rabies, the peculiar symptom satyriasis being very pronounced. Nymphomania has sometimes been noted in women. These symptoms are generally in the stage of excitation, but in the case related above the sexual excitation existed in the prodromic first stage. There was not the least trace of the bite on the hands of this patient.

The most important of all the signs of rabies is the peculiar spasm of the muscles of deglutition and respiration, which makes its appearance when water is presented. The water is dreaded because it suggests *immediately* the act of swallowing; food requires a precedent mastication. Air from a fan, from a window, from opening or closing a door becomes dreaded because of its producing convulsions. It is called aërophobia. The duration of the hydrophobic paroxysm is very variable, the spasms are short in duration and rarely extend over a space of time greater than from one-half to three-quarters of an hour. They come on suddenly. The quiet in-

tervals are at times brief and hardly observable; at others they are prolonged to several hours. The intensity of the paroxysm is influenced by the sex, age, and individuality of the patient and by the mode of treatment. In females and children the attacks are milder. The patients can be quickly quieted by a quiet manner and voice. Their excitement is increased if those about them are agitated or if force be resorted to. Sometimes the paroxysms are completely absent. In their place is dyspnœa and deep sighing in the attempt to swallow; at other times the patient complains merely of great anxiety and obstructed respiration, and it is only shortly before death that a few convulsions take place. In exceptional cases the patient is able to swallow fluids during the whole course of the disease, although the act is painful. Having been unable to swallow, the ability to do so returns and excites delusive hope of recovery. It often happens that he can drink with an effort, however, if he be not looked at, if those about him go away, if he closes his eyes, or if he sucks through a straw or tube. Warm drinks, milk, soup, and also wine, are often more easily taken than water. In by far the most cases there is inabil-

ity to swallow anything. The attempt causes attacks of suffocation, respiratory spasm, and also spasm of the muscles of the face and neck and of the whole body, together with great mental disturbance. There is inability to take solid food, except, at times, with great difficulty. The spasm of individual muscles and of the muscular system in general is usually of a clonic character; rarely are there tetanic convulsions, and a decided tetanus or trismus has never been known. In the intervals between the attacks the intellectual faculties and consciousness remain as a rule unimpaired, although the tone of the voice may be much suppressed, the patient extremely anxious, disturbed, and talkative. There is insomnia except under narcotics. The intellectual faculties are in some cases disturbed. They see objects, animals, and men that are not present and hold imaginary conversations. They imagine that others are responsible for their illness or they energetically defend themselves against imaginary insults and assaults. In a case in which there were marked priapism, erection, and emissions with voluptuous sensations, the patient in his delirium bitterly reproached his medical attendant for having recourse to witchcraft,

in order thus " to take away from him the very principle of life." The disease of this man had set in with a fearful spasm as he was about to wash his face. He was a soldier and had been bitten 40 days previously by a very small dog that had entered the barracks room.

The patient's range of ideas is very limited, bringing forward the same ideas in a short space of time in the same manner. Maniacal attacks are in many instances attributable to rough treatment and attempts at restraint, or they are the result of the horrible anxiety and distress caused by the feeling of suffocation. The attempts to bite are merely actions of despair. The eyes, conjunctivæ, are injected, pupils dilated, and retina hypersensitive to light; the expression may be wild, agitated, excited, or stupid and dull. The pulse is full, moderately strong, and accelerated, becoming weaker and quicker after the paroxysm. The skin is moist and perspiring. Respiration is normal during the intervals, but in the paroxysms it is gasping, irregular, rapid, and dyspnœic. The convulsive respiration is like that produced by a cold-water bath and is regularly attended with throat spasms; these come on together or the respiratory difficulty may

come first. Thirst is decided and there is burning pain in the throat; the appetite remains frequently unaffected; the tongue is usually moist and clean. Sometimes there are convulsive eructations, vomiting of a coffee-ground substance; constipation is usual. The amount of urine is small, never contains albumin, but sometimes sugar is present. The duration of the second stage is seldom as short as one day or as long as four.

The third stage is usually so short as to suggest a doubt of its presence. The fatal termination may take place very soon after the coming on of the severe convulsion. Death may be preceded by a state of general paralysis; this state lasts from 15 minutes to a half-hour. The transition from the second stage is quite gradual, the convulsions becoming feeble and then ceasing. The patient is oppressed with forebodings of impending death. Consciousness remains until just before death. Death may take place suddenly in a convulsion from asphyxia, or quietly comatose. Some patients just before death are able to drink freely. The temperature rises as in tetanus and may increase for one hour after death up to 43° C. " Death is due to paralysis

of the respiratory and circulatory centres. Rabies in man may be confounded with hysteria, tetanus, epilepsy, delirium tremens, and acute mania, also with uræmia. In rabies the temperature is said to rise, as death comes on; in uræmia it always falls. The type of the convulsions, the mental disorder, the abnormalities of general and special sensibility are very different in the two diseases" (Suzor).

There is such a thing as pseudolyssa, lyssophobia, and it may occur in those who are the subjects of some grave disease of which they die, and the deaths are ascribed to lyssophobia —in other words, they are frightened to death. We may be sceptical as regards cases which are reported to have died of lyssophobia pure and simple. In certain forms of neurasthenia the subjects imagine they have any disease that is brought to their notice; every lecturer on medicine is familiar with these cases in students. In a lachrymose way they tell us that they are sure they are taking rabies and they cannot swallow, yet the stomach tube is easy of introduction. But to do this in a really rabic patient is apt to result as follows: My clinical assistant, says Trousseau, with the aid of several pupils, introduced an

œsophagus tube through the nares into the stomach. About 7 ounces of broth were gently poured into it. Half of this had reached the stomach when the fluid suddenly ceased to run. The tube was compressed by violent spasm of the pharynx and œsophagus. The spasm spread to the respiratory muscles; the face turned livid, the open eyes stared. The tube was quickly removed, and as the patient who had been sitting on a chair slipped down on the floor like an inert mass, it was thought that he had died. Water was sprinkled in his face, his tongue drawn out of the mouth, which was kept open by firmly drawing down the lower jaw; the thoracic walls were alternately squeezed and left to expand. A whistling inspiration then followed, compression of the chest was kept up, and respiration was soon reëstablished, after which the patient ejected to some distance a quantity of saliva or bronchial froth. During the paroxysm there had been erection of the penis with ejaculation. The patient evinced no fear on finding himself lying on the ground. He knew that he had just run a great danger, but he believed that he had been saved. In the course of the evening he had several convulsive paroxysms

and died suddenly. A post-mortem examination was made next morning. The body was very rigid, the face livid. The brain and parenchymatous organs were congested. The mucous membranes of the mouth and pharynx were very markedly injected. The salivary glands and saliva taken during life were sent to Alfort, but the dog inoculated took no disease.

PSEUDORABIES, LYSSOPHOBIA.

A mayor of one of the French departments informed Trousseau that he had had rabies. A farm dog had tried to bite his arm, and had bitten a good many beasts which afterwards died of rabies. On Easter Sunday at breakfast, at which he had done his best to make up for a rigid Lent abstinence, the mayor suddenly exclaimed that he had hydrophobia. He could not eat or drink any more and was already beginning to rave when his wife, who believed that he had eaten too much, persuaded him to tickle his throat with his fingers. Copious emesis took place and nothing more was said about rabies.

Trousseau related the case of this gentleman to a judge, who thereupon said that he also once imagined that he had hydrophobia. Riding on

horseback one day, his favorite dog jumped up and kissed his hand; then he ran after sheep, biting all he could. He still heard and obeyed his master's call, but he had a strange aspect. Again he ran after and bit dogs, cows, oxen, swam a river, and died in a few hours. The judge heard that several of these animals died of rabies; he then remembered that the dog that same day had several times licked his right hand. On examining his hand he found several small scars upon it, and upon this was seized with terror. He no longer dared to touch water, to shave himself, and fully believed that he had hydrophobia. A physician tried in vain to calm his fears, and for several days he was excited and delirious. At last being told over and over again that persons with rabies died rapidly, that his dread of water dated ten days back, and after reading about the duration of hydrophobia, he allowed himself to be persuaded, and his dread of water vanished as soon as he became convinced that he should have died long ago if he had been rabid.

PARALYTIC RABIES IN MAN.

The paralytic form of rabies also occurs in the human subject, though much less frequent than the form just described; it is not extremely rare. The following is one of some 30 cases, reported by Dr. Gameleïa, of Odessa (*Annales de l'Institut Pasteur,* 1887, Vol. I, p. 64):

Nicholas Schegowitch, aged 12 years, was bitten August 26th, 1886, by a dog (not known to have rabies) in the right hand. No preventive treatment. Patient fell ill on October 4th. High fever, headache; pain in wounded arm, which is much swollen.

October 5th, pains in stomach with vomiting. The following night the patient is restless, talking and walking during sleep. The succeeding days the same condition was noted. Patient, however, is able to eat and drink.

Patient arrived at Odessa, October 8th. Diagnosis: Total paralysis of right arm. Slight facial paralysis on right side and signs of the commencement of paralysis of the respiratory centre. Sighing respiration, heavy inspiration; when a draught was present, hiccough, uneasiness, and fright. Temperature, 37.7° C.; evening temperature, 39° C. Pharyngeal spasm during eating. At times patient has periods of excitement and begins to cry and complain.

October 9th, delirious all night. Free salivation, fully 6 ounces. Towards morning patient is quieter; complains of pains in legs. Temperature, 36.5° C. Paralysis of right leg. Eats apples and raisins.

7 p. m.: Temperature, 38.3° C. Paralysis; can no longer stand, pains in back; at times delirious.

10 p. m.: Paralysis of dorsal muscles, cannot stand; ptosis of left eyelid.

October 10th: From 2 o'clock in the morning patient is calm. Temperature, 37.6° C.; voice extremely weak. In the morning patient takes a cup of tea and some bread. No spasm of pharynx, complete paralysis; at times sees nothing. Delirium off and on. Sees place and scene of the biting; general weakness.

7 p. m.: Great dyspnœa, showing itself by patient opening his mouth, which remains open, the other muscles that close it being paralyzed.

October 11th, the dyspnœa less during the night. Temperature, 37.7° C. Towards morning patient became greatly excited and talkative. Strabismus divergent off and on (left eye ceases to be fixed and turns towards the left). Paralysis of all the muscles of the body. Patient remained immovable until death, which occurred at 4.30 p. m.

The following case is in opposite contrast to the foregoing:

Dr. Sappington did me the honor to call me in consultation with regard to Wm. Glavesky, aged 14 years. This was on February 6th, 1895, about 3 p. m. The lad was on a lounge in a semi-erect posture, supported by his father back of him. His brown irides were widely dilated, but responded to light slowly. The eyes were brilliant, the anterior chamber seemed deep as though overful of fluid. Pulse rapid, tongue clean. He cannot swallow water. Air blown on him, or rubbing his extremities, is abhorrent. He complains of his father's breath on his head; objects to the proximity of those about him, saying that their breath is fetid; hears noises in his ears as of bells; carries on an imaginary conversation with his sisters, who were not present. During or just before a spasm, thought he saw black things and attempted to repel them. He is constantly spitting ordinary saliva, forming little pools about the floor, and for this untidiness he apologizes to his mother. He tears his body with his finger nails

in scratching, because of intense itching, which he also has in his nose. At intervals of five or ten minutes he has a clonic convulsion, struggling in the arms of his father, this passes off with rigidity of the extremities, stretching himself tetanically for an instant; does not seem to have lost consciousness. Afterwards comes a period of remission. He gets up off the lounge, adjusts his clothing, shakes hands with his visitors; remarks to me, "I thank you for coming to help my father." He walks about the room, goes to a window, and waves his hand to a neighbor. To his pastor asking to visit him, he replied, "I will, if I live." He puts his hand to the back of his head and says he has pain there, also in his epigastrium and hypochondria.

On February 1st, he had complained of stiffness at the back of his neck.

On February 2d, said he had headache.

On February 3d, he went to church, but he had headache, stiff neck, some choking gasping, and short breath.

On February 4th, has been lying down at times; had slight cough, pain in epigastrium, could not eat or drink, but attended school.

On February 5th, tired, wanted to sleep, starts, restless, spitting.

On February 6th, between 1 and 2 p. m., fell down. This tendency to fall is remarkable, and occurs in animals as a result of incoördinate muscular action present in rabies. This night he died after convulsion. Strange contradiction of signs and symptoms! Looked at in the light of fear, he was very ill; viewed in the light of hope, his condition did not seem desperate. "Our hopes belied our fears, our fears our hopes belied." He had been bitten by a stray dog on the right hand, dorsum, and thenar eminence, about November 24th, 1894.

This case bristles with peculiar signs which one may assort for one's self.

The following case is somewhat like that of Dr. Gamaleïa. It is one of the Baltimore cases hereinbefore mentioned. I had the honor to see this case by invitation of Dr. C. H. Mitchell and in company with Dr. R. B. Norment:

Conrad Eppers, aged 15 years, was bitten on back of the neck (wounds severe and multiple) on December 1st, 1896. Underwent Pasteur treatment in New York. Date of first treatment, about 50 hours after the bites. Discharged from treatment December 17th, 1896. There had been no efficient cauterization of the wounds. He died of paralytic rabies December 26th, 1896, nine days after termination of the treatment. Dr. Mitchell saw him on December 23d, 1896. He was quite nervous, but being naturally so this was not regarded. On December 23d he was found to have marked facial paralysis, dilated pupils, and unsteady gait. I saw him on December 25th, 1896; he had complete ptosis of left eyelid, he could not shut his mouth, he could not inflate his cheeks, could not whistle, could not expectorate, but continually thrust a handkerchief into his mouth in order to mop up and remove the excessive salivary secretion. Attempting to walk, his feet would swing about in an incoördinate way. He had had pain in the wounds on his neck. When asked to drink water, he evinced no dread; he simply refused and said that he would not try. His countenance expressed deep gloom; whether due to paralysis of the muscles of expression or a reflex of his mental condition was not determined. Dr. Norment stepped behind him, out of his observation, and fanned him gently; instantly he sprang from his chair in terror, struggling for breath. As the spasm passed off he took a long, sighing inspiration. His physician saw him two hours before his death, and reports that he had at no time

convulsions, but was simply in a paralytic condition. He also vomited almost incessantly during the afternoon. Dr. Mitchell remarks that in both cases (referring also to a lad named Henry, who died from a bite of this same dog) the extremely dilated pupils, the fear of something, the anxious countenance, and the black vomit were noticeable signs; this vomit was copious in another lad named Perry just before his death, at which time I saw him. It is like the vomiting which takes place in septicæmia. I have observed this dark fluid at times in the stomachs of rabid dogs; it is probably bile. Eppers died of paralysis on December 26th, about 12.15 a. m.

Trousseau, quoting Van Swieten, remarks that in the human subject death always occurs within four days after the first rigor and difficulty of deglutition have set in. Most patients die of asphyxia, but in one man death was not preceded by convulsions or even by struggles, and seemed to result from general paralysis, "as though universal paralysis ushered in death."

The boy Henry, aged eight years, was bitten on his left cheek December 1st, 1896. No efficient cauterization. Date of first treatment, 77 hours after the bite. Date of death, December 21st, 1896, three days after termination of the Pasteur treatment in New York. He had been discharged from treatment on December 18th, 1896. He returned home on Friday, December 18th, 1896. Was not well, very tired, thought he had taken cold. Dr. Mitchell saw him on Sunday, December 21st, 1896. He was rested then, but his mind was in a stupid condition and he did not want to be disturbed. On Saturday he had played about as usual. He came in Sunday afternoon, and his mother noticed that he

was very irritable. He had gotten up early that morning, still complaining of being tired and of earache. Within an hour his symptoms had become extremely aggravated. He would seem to be perfectly conscious, and then in a moment make an irrational remark. He was offered a drink, and it was impossible for him to take it. "He did get down one swallow with a terrible gulp." On the next day he looked like a child that had been ill for a great while.

When I saw this child, who was a bright, brave little fellow, he said to me: "I suppose you have come to kill me. I suppose all the boys must be killed." This was the result probably of conversations held among the boys relative to what would be done with them should they go mad. He was delirious one instant and rational the next. His condition of tremor and excitability verged on convulsions. He was asked to try to drink a mixture containing bromide of potash and chloral. He did try; as his trembling hand carried it to his lips, with eyes staring and muscles of his face working spasmodically, he did get some drops into his mouth, remarking with great satisfaction: "Yes! yes! I did swallow some of it." This was about 11 p. m. He died the next day at 5 p. m., after a severe convulsion, of which he had had previously quite a number. The rapidity with which death supervenes after the oncoming of nervous symptoms is remarkable.

The two foregoing cases and the following case were experimentally demonstrated to have had rabies by inoculation of emulsion of the medulla oblongata subdurally into rabbits. The case about to be related was attended by William E. Magruder, M. D., and reported by William E. Magruder, Jr., Olney, Md.

Resin Perry, aged 67 years, was attacked February 3d, 1894, in the public road by a small dog, which appeared to be rabid. While actively fighting and running backwards, Perry fell on a pile of stones and continued resistance on his back with the dog over him. He found a slight wound over his left eye, and at the time thought he had received it in his fall on the stones, but soon his eye inflamed and remained very sore for several days, when it gave no further trouble.

After talking with some friends he became somewhat scared, and feared that he had been inoculated with rabies. On April 11th the eye again became much inflamed, pains radiating from it over side of head and neck, followed by pains in the abdomen and limbs. He complained of being unable to sleep and of inability to drink water the night before, although suffering from excessive thirst. On the 13th spasmodic contraction of the diaphragm occurred, and the idea of swallowing became abhorrent. On the 14th inability to swallow was complained of, and even the suggestion of drinking gave what he expressed "a pain in the stomach and takes away my breath," and said if he could only take some medicine which would enable him to drink he would get well. When induced to attempt to drink, he would scream and run across the room, imploring that the water be taken away from him and out of the room, returning soon to the couch, exhausted and out of breath. The same phenomenon was produced when the door blew open and when the physician washed his hands in the room.

Patient frequently expressed surprise at his condition and wondered at the cause, laughing at jokes and joking between the paroxysms. Pupils contracted. Hypodermic injections of morphine and atropine, and tablets of the same were left with directions for their use at short intervals.

On the morning of April 15th the patient seemed more quiet than before, slept little during the night, having numerous paroxysms followed by rational intervals. Respira-

tion labored, and pulse 110. Temperature was only taken once, when it was normal, and this was the day before death. There was no excess of heat at any time perceptible to the touch.

Administered 30 grains of chloral by the rectum and 15 drops of fluid extract of gelsemium, with morphine, gr. $\frac{1}{4}$, and atropine, gr. $\frac{1}{150}$, subcutaneously. Ordered 20 grains of chloral per rectum every two hours until quiet, but after the fourth dose the nurse could not administer it, as characteristic spasms were produced. Chloroform was used, but discarded for the same reason, producing characteristic spasms after a few inhalations. One grain of morphine and gr. $\frac{1}{30}$ of atropine with 15 drops of fluid extract of gelsemium were administered hypodermically, and the dose was repeated every two hours until patient became thoroughly narcotized, since all attendants were afraid of him and he had become unmanageable. Until near the last of the attack there was almost constant spitting of viscid sputa. Seen at 4 o'clock in a profound stupor, pupils slightly dilated, pulse 120, respiration deep and slow, face occasionally twitching, and extremities cold, with muscles completely relaxed. Took no food, but drank a little water on the 15th and 16th, amid spasms and screams. Remained narcotized until 4 a. m. on the 17th, after several doses of the anodyne had been neglected, when he left his bed and walked across the room. Injections of anodyne resumed and repeated in 20 minutes by the nurse, who had become frightened, and continued every two hours until 10 o'clock, when they were discontinued. Stupor returned after 4 o'clock, and he gave no further trouble. At 11 o'clock pulse was 124 and compressible; respiration, 16 and shallow. At 4 p. m. pulse was stronger and stupor less profound, but mouth dry. Anodyne again administered and repeated when indicated until his death at 12 p. m. on the 17th. There was no general spasm.

A section of his medulla oblongata was sent

to Dr. Keirle, of Baltimore, who makes the following report. Trephined and injected subdurally two rabbits on April 19th with emulsion of medulla oblongata of Resin Perry rubbed up in bouillon; both rabbits developed rabies on May 3d, and both died May 6th.

PARALYTIC RABIES.

The quotation by Suzor of Gamaleïa's cases of paralytic rabies exhibits the following symptoms. These cases are generally a result of deep and multiple bites. Large quantity of virus. Onset by strong fever, general malaise and aching, headache and vomiting, as in all acute infectious diseases. Such an onset is very frequent also in ordinary rabies. At a certain period of the disease there is a high degree of fever; as the disease goes on there is an occasional morning remission and evening rise, but the temperature not a great while before death may rise above normal, and thus persist up to the time of death, and rise somewhat afterwards; or at the time of death the temperature may be almost normal, 37.7° C. The characteristic temperature fall which occurs in the rabbit experimentally inoculated subdurally, and which with very rare ex-

ceptions continues up to death, is not the thermal phenomenon of paralytic rabies in the human being and not that of rabies in general in the human species, in which, though a fall below normal may occur during the course of the disease, it is more of the nature of remission, for it rises again and registers even more than 40° C., and progressively mounting to this degree indicates impending death (M. Schaffer, *Annales*, Vol. IV, p. 313). Subsequent to this advent comes a train of localized pains, generally in the limbs bitten, and girdle pains at different heights of the vertebral column. These localized premonitory pains are rare in the lower limbs. Next supervene a degree of numbness of the senses, fibrillar contractions, ataxy, paresis, and then paralysis more or less complete of the muscles first implicated. General sensibility remains intact, or if it disappears it does so very much later. Then the paralysis spreads, preceded or accompanied by sharp pain in the muscles invaded; the remaining limbs, the trunk, the rectum, the bladder, the face, the tongue, the eyes, are all paralyzed. So also, sooner or later and more or less completely, the respiratory centre, the implication of which brings about a marked

change in the inspiratory phase of the patient's breathing; and as a corollary, some difficulty in swallowing liquids (the so-called great symptom of hydrophobia, or horror of water, being a result much more of the imagination of the patient and of the medical man than of the rabies virus). But this author must not be misunderstood as saying that the incoördination and spasm of the muscles of deglutition and respiration in rabies is imaginary; it is a fearfully real choking, and anything that suggestively calls into action these muscles is avoided and dreaded by the patient. When well marked this respiratory lesion is the cause of dyspnœic convulsions in the muscles which are not yet paralyzed. Then there is frequently a return of the breathing to the normal, but with it is a spread of the paralysis to the heart and death by syncope. This form of rabies has a duration of seven and a half days on an average.

PATHOLOGY.

The gross pathology of rabies presents nothing of specific character, nothing that is not usually present in death from infectious diseases. In man and dog certain gross lesions correspond.

Pial hyperæmia. Cerebral and pulmonary œdema. Vascular injection of upper part of œsophagus and of larynx and trachea; the latter is, however, often not well marked, and is not the cause of the altered voice, which is of nervous origin. The follicles of the tongue and pharynx are not infrequently enlarged; according to Virchow, this is quite frequent in rabies in man. The pharyngeal follicles and lymphatic glands in the neighborhood of the jaw are swollen. The pharynx and epiglottis are usually of deep red color, but are often also quite normal. The lungs are studded with points of atelectases and hemorrhagic infarction, together with sanguineous effusions beneath the pleura. In the dog there were areas of lobular pneumonia due to foreign matter inhaled. Klebs found intense redness of ulnar and axillary glands, jugular, inguinal glands, the tonsils, and lingual glands. Peyer's glands, as a result of swelling and redness of the outer follicles, presented a peculiar wall-like appearance. Upon microscopic examination there was found in all the swollen portion of the lymphatic, and particularly in the submaxillary gland, a deposit of finely granular, highly refractive corpuscles, of faint brownish color,

closely packed together in clusters, at some points in the form of long rows, in others branching out so as to form large star-shaped figures, following in general the course of the blood-vessels. These corpuscles, according to Klebs, may prove to be the vehicles for the transfer of the specific infecting material. This is an unsustained inference; these bodies are probably the result of granular degeneration and subsequent change. The hyperplasia, granular degeneration, and ecchymoses are present in rabies in lymph structures, but they are present in other infectious diseases, as has been before noted in the case of septicæmia in the cervical glands in the dog in the experiment previously detailed. In discussing pathology it is necessary sharply to differentiate matters of fact and matters of inference. The former, making some allowance for imagination and bias, are correct—so far as they go; they are up to date at the time of the investigation; but the latter can never be accepted at any time, except upon a basis of thorough experimental demonstration. These remarks have an application in the kidney in rabies, especially in that of the dog, in which the kidneys are livid and of a dark grayish-blue color. The inner zone

of the cortical substance is usually marked by turbid yellow stripes, the result of fatty degeneration—a normal condition in the dog's kidney. The epithelium in the convoluted tubules is opaque and undergoing molecular degeneration. There is also albumin in the urine. From these appearances Reednew inferred that the pathological phenomena in rabies were results of uræmia. The dark blue cyanotic renal color is common in poisoning by alcohol and opium. In the human being the kidneys are hyperæmic, cortex swollen, slightly opaque, and cyanotic. The bladder is usually empty. Bollinger sums up the appearances as follows: Blood dark. Œdema of brain. More or less pronounced catarrhal alterations of the mucous membranes, especially of the respiratory and digestive canals, conjoined often with hyperæmia and ecchymoses, hyperæmia and cyanotic discoloration of the parenchymatous organs; in dogs absence of food and presence of indigestible foreign substances in the stomach and intestines, together with emaciation. In herbivorous animals there is absence of all characteristic changes. In cattle the morbid appearances are often similar to those of cattle plague.

Suzor gives the following post-mortem appearances in rabies in the dog:

Dark blue and almost black color of the tongue and of the whole mucous membrane of the mouth. In the stomach some discoloration of the lining membrane; black liquid like coffee dregs and heterogeneous materials, not usually swallowed by healthy dogs, constitute the contents of the stomach. Some claim that these foreign substances are present in every case of rabies; another authority says 50 per cent. Congestion of the lungs and of the central nervous system and extreme retraction of the bladder are frequent, but by no means constantly present or characteristic. The hard palate of the dog's mouth is very often pigmented and must not be mistaken as significant.

The foregoing description has a practical outcome in enabling one to answer the question, Is this dog mad? The dog in question has bitten other dogs and human beings; shall the former be destroyed, and what shall the latter do to be saved? You cannot wait 15 or 20 days until the result of trephining or other method of animal inoculation matures; very exceptionally this may be postponed for 90 days. If there be foreign

matter in the stomach; if the lymphatic glands show ecchymoses; if the medulla oblongata, hardened in alcohol and stained with aniline red or other stain, exhibit the knots of hyaline degeneration about the vessels and in the cells regarded by Babes as characteristic—if all these appearances are present, there can be no reasonable doubt; if any one of them be present, or if the suspected dog or other animal has escaped, treatment should be advised. Should the experiment demonstrate that the dog was not mad, it is a mistake barren of consequences; on the other hand, if the dog be proven to have been mad and those bitten be advised against treatment, it is a mistake that may be followed by a train of calamity.

Post-mortem examination in man reveals the following lesions: Cerebral œdema, pial hyperæmia, redness of the membranes of the medulla oblongata and cord, sometimes decided softening of brain, medulla, and cord. The lungs are red, congested, here and there the seat of small hemorrhages, filled with frothy mucus formed at the time of death. Interstitial and subpleural emphysema. These pulmonary lesions, like the liquid black state of the blood, seem to be the

result of the terminal asphyxia (Suzor). Hemorrhages into the muscular tissue of the heart, parenchymatous nephritis, congestion and swelling of the lymphatic glands, with the terminal leucocythæmia, softness of the spleen and liver, with fatty degeneration of the latter—all these are the well-known lesions of infectious intoxication.

Post-Mortem Examination.—The following is the post-mortem examination of the lad Robert Henry, aged eight years, his case heretofore referred to. The examination was made within an hour after death. He died in convulsions.

Inspection: Height, 3 ft. 9 in. Weight, 65 pounds. Rigor mortis absent. Pupils, 8 mm. diameter.

Section: Head—free bleeding on incision of scalp, also from the vessels on removing calvarium. Veins of pia and sinuses much engorged, cerebral œdema, hyperæmia and extravasation of capillaries of medulla oblongata and cervical cord. Pial vessels, veins, and capillaries very hyperæmic; here and there extravasations. Cortex on section darker than normal; vascular puncta marked. (He died at 5 p. m.; at this time, 7.30 p. m., it is noticed that rigor mortis is beginning.)

Body section: Subcutaneous fat absent. Pericardium contains 10 c.c. pale straw-colored fluid. Heart firmly contracted (rigor mortis [?]) and almost empty. Two drachms of blood in right auricle. Small amount of dark, partly clotted blood in left ventricle. Very little in right ventricle; dark red clot in pulmonary artery. Lungs —marked hypostatic congestion; on section ooze bloody fluid freely, intense venous hyperæmia. Stomach—dark-colored fluid. Liver—limited yellow area (fatty degeneration), common appearance in septicæmia. Gall-bladder full. Kidneys hyperæmic. Pancreas apparently normal. Spleen dark red, moderately firm. Œsophagus normal. Larynx and trachea normal, except that the latter is too pale, indicating perhaps intense hyperæmia during life. Bladder empty.

Conrad Eppers, aged 15 years. Case herein previously referred to. Post-mortem examination 12 hours after death, which was caused by paralysis of some vital structure.

Inspection: Height, 5 feet 4 inches; weight, 130 pounds; rigor mortis marked.

Section: Free bleeding from meningeal vessels; extravasations along longitudinal sinus; also free bleeding from pial vessels, which are

very hyperæmic. Cerebellar cortex, on section, dark; cerebellum softened. Veins in vertebral canal very hyperæmic. Lungs œdematous, pit on pressure, ooze freely bloody fluid. Heart—one ounce of fluid in pericardial sac; coronary arteries full of blood. Dark fluid blood in right auricle; very little in right ventricle; left ventricle empty. Spleen—6 x 2½ x 1½ inches. Liver apparently normal. Kidneys very hyperæmic. Pancreas hyperæmic. Larynx contains frothy fluid; œdema over arytenoid cartilages.

The foregoing post-mortem examinations exhibit nothing specifically indicative.

Microscopy of the Nervous System.—For the following microscopical examination of the nervous system and other tissues of the dog and the boy Henry, the writer has the honor to be indebted to Dr. Standish McCleary, associate professor of physiology, College of Physicians and Surgeons, Baltimore. In the gray matter of the cervical cord of the dog there is hyperæmia and extravasation; also escape of polynuclear leucocytes into perivascular lymphatics. Granular degeneration of ganglion cells. In the nerve fibres the medullary sheath of Schwann is swollen and hyaline through the entire section. In

the kidney blood is extravasated into and between the tubes; also from the glomeruli. The cells of the uriniferous tubes are very much enlarged and finely granular (cloudy swelling). The intertubular vessels are hyaline, and small round cells are proliferated in the connective tissue here and there. The lymph glands exhibit abundant blood extravasation; those in the axilla have the leucocytes pigmented occasionally. In the boy Henry the ganglion cells of the medulla oblongata are swollen and their nuclei granular, and the adjacent protoplasm is hyaline; hyperæmia and minute extravasations in gray matter (dorsal accessory nucleus, olivary body). Same condition of hyperæmia and extravasation in the white matter (formatio reticularis). The vessels are hyaline, and there is extravasation of polynuclear leucocytes.

Suzor states as follows: On post-mortem examination the lesions of main interest are found to lie in the central nervous system. The nerve cells are cloudy and granular; general congestion of the nerve centres, the blood-vessels being dilated and ruptured here and there, giving rise to small hemorrhages; miliary abscesses throughout the substance of the medulla oblongata, more

sparsely in that of the brain and cord; foci of finely granular matter infiltrating the normal nervous element, the perivascular lymph spaces, and the walls of the blood-vessels, which are compressed and assume a moniliform or beaded aspect; hyaline thrombi or blood clots form in the interior at the level of these compressed points, the whole giving the appearance of a nodule or small tubercle, in the interior of which Klebs thought he had discovered the specific micrococcus. There is frequently softening around the central spinal canal. Ross, of Manchester, finds that the lesions here are most marked, but the anterior and posterior horns and the gray matter throughout are largely implicated also, mainly so perhaps. He thinks there is similarity between the lesions of tetanus and rabies. In the former they are chiefly spinal; in the latter cerebral in their main localizations. This observation is perhaps not sustained. The ganglia of the sympathetic system and of the nerve roots show the same lesions as the brain and cord. The nerves, and in particular those of the bitten parts, those rising from the medulla, the vagi, the glossopharyngeal, the hypoglossal, the spinal accessory, the phrenic,

have been found red, hyperæmic, swollen, and the seat of minute foci of hemorrhage; the myelin is diffluent, fragmented, and in many nerve fibres the axis cylinder has altogether disappeared.

William H. Welch, M. D., professor of pathology, Johns Hopkins University, gives the microscopical appearances as follows:

Serial microscopical sections of the medulla oblongata and pons from the second cervical nerve upwards exhibit small hemorrhages and accumulations of small round cells in large numbers, both in the perivascular lymph spaces and in scattered foci in the neuroglia between the nerve elements; hyaline thrombi and leucocytes in the small blood-vessels. These lesions were microscopical, and their extent and distribution could be determined only by the examination of a large number of sections from different parts. The lesions were especially well marked in and near the nuclei of origin of the spinal accessory, pneumogastric, and glossopharyngeal nerves, and in the motor nucleus of the trigeminus. Cases have been reported in which even more extensive lesions than these have been found, their intensity depending apparently in large measure

upon the duration of the disease. While it cannot be claimed that these lesions are peculiar to hydrophobia, or by themselves suffice for its diagnosis, it is incorrect to suppose that hydrophobia is a disease without demonstrable anatomical lesions which bear a manifest relation to the symptoms of the affection.

M. V. Babes, treating of the histological lesions of rabies, notes the hyaline degeneration of the vessels and the presence of miliary nodules around the vessels and cells—"la présence des lésions décrites et surtout des nodules pericellulaires parle en faveur de la rage de l'animal suspect" (*Annales de l'Institut Pasteur*, 1892). He also refers to inflammatory lesions, especially of the vascular tunics. Some of these lesions are visible to the naked eye, but usually they are not.

Dr. N. Gamaleïa gives the macroscopic lesions in the nervous system:

Ismael Ivanoff, aged 45 years, bitten on June 15th by a mad wolf. Numerous wounds on the head and limbs. The precursory symptom of the disease (slightly sighing respiration) was present on July 2d. Twenty hours after there is difficulty in swallowing liquids. Vertigo.

July 3d, anguish and agitation; towards evening there is great muscular feebleness, very pronounced in this robust man.

July 4th, death by asphyxia and convulsions.

Autopsy: Spinal marrow—dura mater is unchanged. The pia mater is very hyperæmic; the tissue at the upper part of the cervical enlargement is very succulent—it oozes out on the surface of the section. The lateral columns present a softening of a gray color almost throughout their whole extent. In the upper end of the cervical enlargement the softening is more manifest on the left; at the inferior end it is more marked towards the right. In the dorsal portion the softening is more limited. The lumbar enlargement is soft, succulent, and hyperæmic.

Andre Doinik, aged 14 years, bitten on the face by a mad dog four weeks before the disease. The patient had not undergone preventive inoculations.

February 16th, dread and refuses to eat.

February 18th, hydrophobia, aërophobia. Muscular agitation. Died at 11 p. m.

Autopsy: Pia mater is very hyperæmic. One observes in the cervical enlargement on section the irregular contours of the gray substance of the posterior horns, especially the right; this is due to the formation of gray islets in the white substance, islets which unite themselves to the posterior horns. In the lateral columns at the right there is also found a gray focus of the size of a pin's head. Elsewhere the medullary tissue is less consistent, and in the gray substance there is hyperæmia.

Dr. Henry J. Berkley, of the Medical School of the Johns Hopkins University, replied to my request for information regarding the lesions of rabies in the rabbit's brain as follows: "The lesions in the four hydrophobia rabbits I have studied are entirely similar to those resulting from other irritant poisons, but resemble more

the alterations in chronic serum poisoning than anything else I have studied—namely, a peculiar swelling of the dendrites of the nerve cells, with loss of the gemmulæ, and eventually atrophic changes in the corpus of the cell." The article above referred to is remarkable and may be found *in extenso* in the Johns Hopkins Hospital Reports, Vol. VI, No. 1; "Report in Neurology," III, 1896; Part IV, "Hydrophobic Toxæmia," I, "Lesions of the Cortical Nerve Cell Produced by the Toxin of Experimental Rabies."

In this article Golgi is quoted as follows: "In both cell body and dendrites there are evidences of decided alterations, in the form of circumscript or diffuse swelling, atrophic changes with loss of substance, a process of progressive atrophy which proceeds apparently from the cellular body to the finest extension of the protoplasmic branches. The processes are involved to their extreme periphery. The cells lose their homogeneousness, have a granular appearance, and show diffuse swellings which give them a varicose appearance. There is also an involvement of the axis cylinder in the form of a beaded swelling of the fibre. A peculiarity of the process is that the abnormal alterations of the ele-

ments are not diffused throughout every portion of the central nervous system, but they are focally distributed; thus one sees zones with altered cells and others without alteration of the nerve elements."

"Golgi," Berkley remarks, "is evidently inclined to think that the alterations above described are pathognomonic of rabies and that they are due to an inflammatory process, and gives this the name encephalomyelitis parenchymatosa." There is no inflammatory process set forth in the foregoing quotation from Golgi. Dr. Berkley remarks further:

"As regards the vascular system I have failed to discover in the cerebral cortex of the rabbits any evidence of coarse lesion of the vessels in the form of extensive hyperæmias, plastic exudates, and extensive emigration of corpuscular elements into the perivascular sheaths, nor could a single extravasation of the red corpuscles be found as described by Popoff (Virchow's *Archiv*, Bd. 122) and others in the human subject. None of the cortical vessels of the rabbits' brains showed more than a moderate filling of the capillaries, and but a trifling emigration of the polynuclear elements, and no extravasation of plastic

exudate of any description. The perivascular spaces are only moderately wide, contain a comparatively small amount of finely granular débris, no hæmatoidin crystals, or indeed anything beyond a few lymphoid corpuscles. The latter elements are but sparingly present in the blood within the walls of the canals. The sheaths of the vessels are not greatly altered, the endothelial nuclei are not swollen, some of the nuclei of the muscularis show a tendency to absorb less of the aniline stain than usual and show vacuoles, but the muscular fibres are not swollen or hyaline, and, altogether, the evidence of a degenerative process taking place in the walls of the nutrient vessels is inconsiderable.

"We have, therefore, in the present cases only the indications of a mild infection, of sufficient intensity, it is true, to cause death after the lapse of a considerable number of days, but insufficient to produce any considerable morbid change of the vascular walls, together with a degree of leucocytosis such as is often found when the soluble poison of bacterial source acts with a considerable degree of energy upon the blood-forming organs.

"These conditions are therefore most favor-

able to enable one to ascertain the effect of the subtle poison from the rabies bacterium upon the nerve elements. Golgi's cases, in which he found karyomytosis of the nuclei of the vascular muscles, must have been of greater severity, and the damage to the nutrient supply has borne its part in the production of the nerve-cell changes, which we are now able to exclude to a certain degree.

" I can see no signs in any of the preparations of anything approaching an inflammatory process taking place in the cerebral tissues, only the indications of a purely degenerative reaction from the effect of a toxic substance produced by the bacterium of hydrophobia, essentially causing the same pathological changes as those induced by other soluble poisons when present in the circulation in sufficient quantity to disturb nutrition."

It must be borne in mind that Dr. Berkley is writing of the cerebral cells and cortex in rabies in the rabbit; if this rabbit was obtained from me the virus was probably fixed. It is necessary also to remember that the bacterium referred to is a supposititious (hypothetical) one. That the rabies virus, be it what it may, is phlogistic

is by no means certain. The appearances, conspicuous as they are, macroscopically or microscopically, are susceptible of explanation independent of inflammation. Toxineurosis, if the word may be applied to the organic changes produced in the nervous system, can independently and directly produce coagulative necroses. Infectious intoxication is not necessarily inflammatory or in this way toxæmic. So far as rabic intoxication is in question, the blood stream is only very transiently a carrier of it; only exceptionally and by inoculation of large quantities can rabies be produced by the blood. The virus of rabies can kill the protoplasm of cells and the vessel wall. Whether the latter is killed from within or from the tissue and lymph stream without, is a question in which experiment does not favor the former route. The hypothetical bacterium and its toxin are repelled by the blood. How does the blood deal with rabic virus when injected into the blood-vessel? This point may be approached digressively by a passage from Suzor: "M. Bouley remarked to Pasteur, 'Perhaps there is no such thing as a microbe of rabies.' 'All I can say,' replied Pasteur, 'is this, that if you were to bring me two

brains, the one rabid and the other healthy, I could say from a microscopic examination of the two medullas, this one is rabid, that is not. Both show an immense number of molecular granules, but those in the rabid medulla are finer, more numerous, suggesting the idea of a microörganism of extreme tenacity, in shape neither a bacillus nor a diplococcus; they are like simple dots.'

"One method alone hitherto has allowed us to isolate these granules from all the other elements of the nervous matter. It consists in injecting the pure virus taken from the medulla of an animal which had died from hydrophobia into the veins of a rabid animal just at the time when asphyxia is coming on. In a very few hours the blood of the animal is found to contain exclusively the infinitely small granules we are speaking of, the normal elements of the nervous matter having either been stopped in the capillaries or having, more probably, been digested in the blood. It has also become easy under these new conditions to stain them with the aniline dyes."

With regard to the blood of rabid animals we have in one instance been able to give hydro-

phobia to a dog by means of the blood of a rabbit which had died of that disease. The granules in the blood described by Pasteur are not organisms, they may be the means by which the blood deals with organisms, the granules of certain leucocytes which destroy them and prepare them for removal by certain other leucocytes, or they may be granular destruction of leucocytes by organisms or their toxic products. These may be the granules described by H. F. Müller.

BLOOD OF RABBIT IN RABIES.

The following is an examination of the blood of a rabid rabbit kindly prepared for this article by Dr. Standish McCleary:

To ascertain what changes if any were produced by the laboratory (fixed) virus upon rabbits' blood, counts were made from healthy animals (rabbits) and from rabbits in the last stages of rabies. Differential counts were made from specimens stained by Ehrlich's triple stain and also by hæmatoxylin and eosin. The results could hardly be otherwise designated than negative. The number of red cells per cubic millimetre in the healthy rabbit was found to be about 6,000,000, while the total number of leu-

cocytes amounted to 7,500. The blood of rabbits in the last stages of rabies showed the erythrocytes reduced to 5,460,000, and the leucocytes to 7,200 per cubic millimetre. The percentage of hæmoglobin was proportionately diminished. This oligocythæmia was to be expected on account of the anorexia and general malnutrition concomitant with the disease. The absence of even the slightest leucocytosis is to be noted as indicating that there is not a meningitis or any suppurative processes in the nerve centres.

Contrast this condition of the blood with that which occurs in the toxæmia of rabbit septicæmia. The following is an account of the condition of the blood in the experiment in which the bacillus of rabbit septicæmia was derived from the medulla oblongata of a supposed rabid dog, herein previously detailed. Special attention must be directed to the dyspnœa which is hæmic, not pulmonary. The lungs are pallid and bloodless, or, more correctly stated, the blood is not red blood, the red blood corpuscles are not red; even when closely agminated the color is only a faint yellow and the single corpuscle has no color at all. Morphologically the

red corpuscles are distorted, fail to maintain their sphericity, and may, like a globule of mercury, drag a tail; in addition to this poikilocytosis there is a pseudo-nucleation caused by a circumscribed absence of protoplasm (hæmoglobin). This excessive liability to vacuolation of the corpuscles is general and takes place in different parts of the area of the cell. Sometimes the cell is emptied of its contents, the periphery alone as a mere ring remaining; sometimes, as just noted, a zone between the circumference and the centre is vacuolated, leaving the centre as a seeming nucleus; the term excessive liability has been used advisedly, because all vacuolation occurs as a post-mortem change, and as a result of reagents, especially acid stains (dyes); but this disintegration described, this granular necrosis, this proneness of protoplasm to drop out is an *intra vitam* result of this organism, a pernicious anæmia.

DIAGNOSIS.

The complete picture of furious rabies in the dog is not difficult of recognition. Unusual forms and paralytic rabies may escape the detection of the most careful and experienced vet-

erinarian, who for its solution is compelled to resort to experimental demonstration.

In general, in man, continuous observation and a good clinical history obviate error. In rabies, as it occurs usually in the human subject, it is difficult to confound it with any other disease. A most distinguished clinician has remarked: "Other diseases may be confounded with true croup, but when you see your first case of true croup, you do not confound it with any other disease." This remark is entirely applicable to rabies, as it generally presents itself. Certain forms of rabies, if observed disconnectedly, may be mistaken. Maniacal rabies, observed only in the maniacal period, may resemble ordinary mania if the foregoing history be disregarded. Hysteria lacks the reflex excitability of rabies. The symptom of black vomit is a late sign indeed, but it may suffice to distinguish rabies paralytica from Landry's paralysis. The usual form of acute tetanus cannot be confounded with rabies, the former supervenes within ten days of the reception of the wound; the sardonic grin is absent in rabies. Subacute tetanus with long incubation often recovers, and its persistent muscular rigidity is unlike rabies. Cerebral

tetanus, caused by wounds in the vicinity of the cerebral nerves, in which spasm of the muscles of the jaw and throat takes place, has the shorter period of incubation; persistent spasm of the jaw muscle (lockjaw) is not a symptom of rabies. Temperature is sometimes relied upon to distinguish tetanus from rabies. A decided rise of temperature in the former is supposed not to take place in the latter, but rabies in man does have a decided rise of temperature which may portend death, as has been adverted to, and the temperature may rise in the rectum after death to 42°. The temperature in human rabies "rises as death approaches, in uræmia it falls below normal."

TREATMENT.

That death must always result in order to prove rabies in man is perhaps an erroneous premise, but no fully demonstrated case of recovery is on record; of course the demonstration of the recovery is contingent upon the demonstration of the disease, which in case of recovery is very difficult. Albutt quotes a case from Lebell and Venesco in a child six years old in whom the disease in a severe form supervened during

treatment, which was interrupted and resumed on its abatement. In the treatment, in addition to the Pasteur series, fixed virus heated to 80° C. (176° F.) in emulsion was used in quantity of 87 gm. At this temperature, and much below, all virulence is destroyed. In the case of an adult male at the Institute Pasteur undergoing treatment paralysis supervened and became general, notwithstanding which the treatment was continued without interruption and the patient recovered. Another case of like character has occurred. These are all the cases of this nature in over 19,000 cases treated during 12 years, 1886 to 1897 inclusive. To the idea that this paralysis was a result of the treatment was opposed the small number of cases in which it occurred. Neurasthenia (hysteria) was suggested, also some toxin other than that of rabies. Again, it was suggested that the paralysis was paralytic rabies caused by the bite and not by the treatment, which having been administered without intermission cured the disease (*Medical Week*).

Suzor quotes Gamaleïa. The virus can only spread by the nerves from periphery or external surface to the centre. The physician ought to cease aiding the virus by morphine; he ought

to help the nervous system. Artificial respiration and strychnine are advised. Rabies is not so common in men as in the dog and the symptoms are not so severe. Yet in the dog cases are on record of undoubted recovery, but they will not be undoubtable until demonstrated. Chloral and curare fail to cure; chloroform, or hydrobromate of hyoscine is used palliatively. An intelligent citizen wrote me: "Do not let the boys one after another die of rabies; give them the brains of rabid rabbits to eat." In such an emergency *de gustibus non disputandum est.* In the light of modern therapeutics this suggestion in the abstract is not so absurd as it seems on first thought.

PROPHYLAXIS.

The death rate of those that have been cauterized is 30 per cent., of those uncauterized it is 80 per cent. Efficient cauterization is by the hot iron, thermocautery, sulphuric, nitric, and carbolic acids, chloride of antimony, acid nitrate of mercury, applied in less than one hour after the bite. Sometimes it is necessary to open up wounds by incision, or even to resort to amputation. Otherwise the wounds are treated as are other infections. Sucking the wound, dry-cup-

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ping glasses, ligation above may under some circumstances be useful preliminaries. But the physician must exercise judgment. Wounds may be so numerous, so lacerated, so sinuous, that it is impossible to cover the whole surface with the actual or potential cautery. Careful washing and syringing with antiseptic solution and the application of water as hot as can be endured (130° F.) "are painful but can be endured." This application of hot water can usefully be made a part of the daily toilet for several months, say three months. Hot bathing, dry or moist air, persisted in throughout the incubative period, are useful adjuvants. Experiments seem to show that enfeebling excesses, especially alcoholic, increase the risk; the latter, some experiments seem to indicate, interferes with the immunization.

What classes of bite shall be subjected to the immunization treatment? All in which the skin, the cuticle, the epidermis, has been abraded, scratched off by the tooth. Cases in which the skin has been merely bruised through untorn, unperforated clothing may be exempt. Whenever and however the saliva, the secretion, the tissues of rabid animals have been applied to denuded

surfaces there is then risk, though it may be slight. Suspected animals that have bitten other animals should not be killed if they can be kept securely. If rabid they will probably die in two weeks, if sick of other diseases they may recover, if vicious they remain well. Should they die they should be investigated by gross and microscopic examination; the latter may be restricted to the medulla oblongata, which should be inoculated into rabbits or guinea-pigs, preferably the former by trephining.

Immunizing prophylaxis may be produced by the Pasteur method in which the antitoxin is made in the body of the animal undergoing treatment. In the method of Babes, of Bucharest, the serum of an immunized dog is used. Tizzoni and Cantanni of Italy use the serum of immunized sheep. In this the antitoxin is formed in another animal and injected into the animal undergoing treatment. The animals immunized with the object of obtaining an antitoxin are not so rendered by the Pasteur method, but by means of a virus attenuated by peptic digestion. Some use a mixed method, partly Pasteur serum therapy indirectly and partly serum therapy directly. The following is the method of immuni-

zation practised at the Pasteur Department of the College of Physicians and Surgeons, Baltimore, Md., and it is identical with that of the Institut Pasteur, Paris.

Select a rabbit that has died of rabies after six days' incubation, having been inoculated subdurally by trephining and injecting, as has been hereinbefore described. The rabbit must not be killed; it must be permitted to die, and its medulla oblongata must be extracted and used before decomposition, the dead animal may sometimes be put in an ice chest, if unavoidable. Lay this rabbit on its belly on a zinc tray (79 cm. long, 54 cm. wide, and the border turned up $2\frac{1}{2}$ cm.); make a cut with a knife or scissors from the nose upwards and backwards along the middle of the head and back to the tail, lay off the skin from the head and from the body down to the tray. With the scissors or knife cut off the muscles in long strips and lay bare the spinal lamina; cut off the spinous processes with scissors. Then thrust the beak of a Liston bone forceps into the orbit, cut the calvarium obliquely backwards; do this on both sides and unite the incisions by a transverse cut behind and in front. The calvarium may then be lifted off, or it may

be removed bit by bit as the operator pleases. All the while the muzzle of the rabbit is held in Farabeuf's notched forceps (the instruments are not devised specially for this work; they may be obtained from Collin, Paris, or skilled instrument makers everywhere). When the brain and medulla oblongata have been exposed, slit the dura and remove them, and place them in a sterilized saucer, base upwards. Cut the vertebral lamina on both sides with the bone forceps from above downwards; be careful not to tear the membranes or the cord. "It requires practice to bare and extract the cord intact, particularly from the narrower parts in the neck and shoulders." Expose the cord for 10 inches, divide it transversely at the lower end, seize the cord and the membrane with a pair of dissecting forceps (toothed), raise it and cut from below up towards the head the spinal nerves which hold it. It may be placed in a sterilized dish or allowed to remain loose in the canal; cut two pieces each 3 inches long and tie a piece of sterilized thread to one end of each piece; withdraw the cotton stopper from the sterilized bottle, and put the piece of cord into the bottle without touching its sides; then put back the stopper which presses

and holds the cord, a part of which is allowed to hang outside. Do the same with the other piece. Put the date on the label of the bottle and also the number of the passage, and also, maybe, the number of the rabbit that has undergone this passage—*e. g.:*

500–3.
June 23d, 1898, 2 p. m.
A.

500–3.
June 23d, 1898, 2 p. m.
B. ×.

These bottles are duplicates, and they are placed on the shelf in the cord room one behind the other. Should a culture from the cord exhibit a growth, a cross × is placed on the label. After the cord has remained 24 hours in the cord room, a piece is cut off and dropped into bouillon in a test tube, which is put in a thermostat and examined after 24 hours. The bottom of these bottles is covered about 2 cm. deep with flake caustic potash, the piece of cord hangs over this, its lower end level with about the middle of the bottle. The glass manufacturers list these bottles as aspiration or irrigation bottles. Their capacity is 1 liter, they are 23 cm. high, 8 cm. in diameter across the bottom; on the side near the bottom is a nozzle opening into the bottle, and the opening has a diameter of 2 cm. The opening in the neck of the bottle has a diam-

eter of 2½ cm. The openings are plugged with cotton and the whole is sterilized in the hot-air sterilizer. These bottles are removed at once to the cord room, which is kept between 20° and 25° C.

From the medulla oblongata floor of fourth ventricle two rabbits are trephined and subdurally inoculated as previously described. A convenient cord room may be constructed as follows: Partition off the corner of a room for a space of 12 or 15 square feet; let the partition be double with a space between, which is lined with thick paper or asbestos. The room should have a window and a door, the latter and the shutters of the former are constructed like the partition; the ventilation should be through the roof. Two shelves run the length of room on one side, the first row, 128 cm. from the floor, is 42 cm. wide; 41 inches above this shelf runs a similar one. A gas burner and two intermediate burners occupy one side of the room. The bottles with the cords are placed one behind the other on the lower shelf, 15 bottles in front and 15 bottles behind. If the culture of the cord from the bottle that has been on the shelf 24 hours exhibits a growth, bouillon be-

comes cloudy, a cross is put on the label; if it be necessary to use this cord it is reëxamined, and often the growth has disappeared. As a rule these growths are non-pathogenic, and cause no trouble when injected; occasionally the green pus organism is present. Such cords are rejected unconditionally, though this organism is itself non-pathogenic. This room is kept dark, door and shutters closed, artificial light only for illumination; in winter a Bunsen or a gas stove with thermo-regulator. The latter is not easily managed and personal attention can sufficiently regulate the flame. The heat above mentioned is sufficient for this climate, in which 0° F. is very rare. If the main room—that which includes the partition—be heated (steam heat), it is advantageous. The summer in this climate does not long remain at 90° F., but when about 84° some refrigeration will be necessary in the cord room. This may be simply accomplished with a mixture of the following proportions: Chloride of sodium (rock salt), 150 lbs.; sulphate of soda (Glauber's salt), 50 lbs.; carbonate of soda, 17 lbs. This is put with intervening layers of broken ice in a tank of the following description: A galvanized iron cylinder with a bottom and a

removable lid, 47 cm. high, 46 cm. in diameter. In the centre runs an open cylinder 11 cm. in diameter through the top and bottom; the bottom of the main cylinder is about 2½ cm. above the ground; the rim of the body of the cylinder which rests upon the ground is perforated with orifices 2 cm. in diameter and 8 cm. apart so that air may have access to the outside surface of the bottom. Fill the main cylinder with interlayered parts of ice and the above mixture, the first layer being ice. A small open nozzle enters the main cylinder at the bottom and is closed with a cork. The cylinder is put in a wooden wash tub and surrounded with sponges. This is placed in the cord room. Moisture which is undesirable is obviated by chloride of calcium, in ordinary pie pans (tinned iron), which, to guard against leakage, are set in stoneware bowls. The room is not frequented; those only enter it habitually who must. It is furnished with a thermometer, registering maximum and minimum. When the floor is swept—which is rarely—wet sawdust is used, and the woodwork washed in alcohol. A day of good temperature and fair is selected, the cords taken into the main room, and the window of the cord room left open and the door shut.

In starting a supply of rabbits and cords, trephine two rabbits daily for two weeks, keeping the cord that is being used in the ice-chest, in a sterilized test tube; in about two weeks the rabbits will begin to die daily, and ever after the supply must be maintained by trephining two rabbits daily. Thirteen boxes with 26 rabbits will be required for this alone; but 25 boxes will barely meet the exigencies of outside experiments in determining whether animals sent you are rabid. The rabbits are fed on a mixture of corn 1 part, oats 1 part, and bran 2 parts, with a little cabbage daily.

In preparing the emulsion with which to inject patients it is better to use the main room, and have a table with a drawer in which are labels, glass rods, curved scissors, and forceps, the glass rods having been wrapped in paper and sterilized in hot air. Erlenmeyer flasks, 100 c.c. capacity with cotton plug, contain water sterilized in the autoclave. There are also stout wine glasses covered with paper caps and sterilized in hot air; the wine glass inside does not taper to a point but has a flat bottom $\frac{1}{2}$ cm. in diameter, which corresponds to the diameter of the glass rods which are 25 cm. long; the wine glass

brimful holds 40 c.c. There is, of course, a Bunsen burner on the table. For the newly arrived patient the cord of the thirteenth and fourteenth day is used; that is, a cord that has been drying over caustic potash for 13 and 14 days. Such a cord measures transversely ½ cm. The cord is for one instant passed into the Bunsen flame, then with curved scissors, previously heated to redness in the flame and allowed to cool, less than a millimetre is transversely cut from the end of the cord and allowed to drop into the wine glass; ten such pieces measure 8 mm. and weigh 20 mgm. This is triturated with the glass rod until it has become thoroughly broken or mashed according as it is recent or old. Then a few drops of water are added and it is triturated until a milky fluid results, then more water added until finally 15 c.c. is reached. The emulsion now looks like rice water and a sediment soon accumulates; the paper cap is put back on the wine glass, and on the bottom rim, upper surface, is put a label with the number 14 on it, meaning a cord that has dried 14 days (older cords, 15-day cords, are rejected and the bottle cleaned). The caustic potash after twice using requires renewal; in 28 days

it looks like wet white candy. The glass rods wear smooth and require to have pieces cut with a file and broken off, thus becoming sharp again. Similar to the above the thirteenth-day cord is prepared in a wine glass. These wine glasses are put in an agateware tray or baking pan in which are placed pieces of filter paper, and a bowl with some 3 per cent. solution of carbolic acid and two Pravaz syringes. A list is made out with the names of the patient and the age of the cords —that is, the number of days they have been drying, and the day of the month corresponding, which is the date on the bottle, and the dose, *e. g.:*

For June 24th, 1898.

	Cord.	Date.	Dose.
George Williams.....	10 days.	June 14th.	3 c.c.
Edward Cook.....	5 days.	June 19th.	2 c.c.

These lists are made out and put on the table the day before the treatment, and are entered in the case book, which records the circumstances of the patient's case, *e. g.,* name, age, seat of bite, number of bites, animal that inflicted bites, cauterized or not, what has become of animal, etc.

The temperature of the cord room and of the outside atmosphere, and the result of the culture

are recorded in a book on the table in main room. We now take the tray and go to the patient. The patient is permitted to stand, sit, or lie down as he or she may desire. The Pravaz syringes and needles, which have been filled with 3 per cent. carbolic acid solution, are emptied and washed out with sterilized water. These syringes, holding 3 c.c., are filled by thrusting a needle through the paper cap of the wine glass; then the abdominal region of the patient is bared and the site of the injection, hypochondria, and anywhere on abdomen, avoiding large veins, is wiped with filter paper wet with 3 per cent. carbolic acid solution. Then the skin is raised in a fold between the fingers and the needle is thrust well into the subcutaneous cellular tissue. It is important to avoid injecting the layers of the skin, which is painful, and to avoid sites of previous injection. After the injection a piece of filter paper wet with the carbolic acid solution is put on the skin and allowed to remain for a few seconds.

We have not modified the dose relative to age. In our youngest patient, a girl two and a half years old, and an old lady aged 84 years, the same doses were given. At times there are red-

ness and induration in the connective tissue, but there has never been pus, never cellulitis of the slightest gravity. Hot-water applications on towels suffice to remove these trivial inconveniences. The treatment occupies 21 days at least.

First day (thirteenth- and fourteenth-day cord) 3 c.c. each at the same time, and so on until the sixth-day cord is reached on the fifth day; two injections of the sixth-day cord emulsion are given in doses of 2 c.c., each at the same time; subsequent injections are: sixth day (fifth-day cord), 2 c.c.; seventh day (fourth-day cord), 2 c.c.; eighth day (third-day cord), 1½ c.c. Injections are not given of cords earlier than the third day. Now begin again with fifth-day cord and come down to third-day cord inclusive; these all now being 2 c.c. doses.

If it be thought desirable to approach at first the more virulent cords gradually, when the fifth-day cord is reached, a fifth-day cord may be given again as the next day's injection; so also with the fourth-day cord, but after this reduplication the course of the injections is resumed and maintained in daily succession, fifth-day cord, fourth-day cord, third-day cord, and over again until the 21 days have passed, the dose being 2 c.c. each time.

By a coincidence the patients that I have observed—46 in number—have markedly improved in general bodily condition during treatment.

It is much to be regretted that a reliable antitoxin is not available to displace the foregoing elaborate technique. Until such shall appear a close imitation of the technique of the Institut Pasteur, Paris, is the only way.

That purging, sweating, hot baths (water, dry air, or vapor), can eradicate rabies once it has reached the citadel of vitality, the medulla oblongata, is incredible, because it lacks experimental demonstration. That dogs, rabbits, chickens, and mice have recovered—the two former from the early stages prior to the development of acute symptoms, and the two latter even from advanced rabies with fully developed nervous symptoms—there can be no doubt, because these have been the subjects of experimental demonstration.

EFFECT OF HEAT ON RABIES.

How do these animals sometimes—for it is very exceptionally—recover from rabies? They heat it out. The hen has a normal cloacal temper-

ature of 108° F. From the moment the virus is inoculated she begins to attenuate it; this is proved by the long incubation, even with fixed virus amounting in some cases to over 20 or 30 days. Notwithstanding all these advantages the hen rarely fails to take the disease and rarely recovers, but she dies game, though vitality has been driven from its citadel; the foe has likewise perished, the virus is sterile, the medulla inert. Recall to mind the experiment of Dr. Byron. Medullas in an incubator for eight days at 40° C. (only 104° F.) gave marked rabies to rabbits, but the animals got well. At 50° C. (112° F.), these medullas produced no disease. At 108° F. the rabic virus in vitrio becomes sterile; at 108° F. in the hen the rabic virus does become sterilized, but too late to prevent rabies, though it is so attenuated as to enable her sometimes to recover. Can the temperature of the human animal be raised in the medulla oblongata to 108° F. and maintained there for eight days? Or can it be raised to 108° F. daily and maintained at that point for a short time safely? To say the least, it is a dangerous temperature for the medulla oblongata of man. To put the *sine qua non* at its lowest terms, can a tempera-

ture of 104° F. be obtained daily for eight days? Can it be maintained for eight days? Let the question of maintenance be abandoned as not feasible, practically very difficult, doubtful. Can a temperature of 104° F. be attained in the human animal once a day for eight days? This is giving odds against a negative result of the experiments, for in Byron's experiment 104° F. was maintained for eight days. The following experiment is not as thorough or conclusive as is desirable, but it elucidates some points regarding the effect of hot, dry air on rabbits trephined with rabies.

In taking the temperature the thermometer must be all its length in the bowel, only enough for holding remaining outside; with the ordinary clinical thermometer this can readily be done even in the guinea-pig. When in the hot-air room the whole thermometer must be within the sphincter ani, otherwise the temperature of the room would affect it. To do this, have a metal-case thermometer and tie a piece of thread around it so that it hangs outside the anus; take the temperature before putting the rabbit in the hot room, then return the thermometer to its case and gently push the whole instrument up

the bowel and inside the sphincter, retain it by a compress over anus and a tailed bandage. When man is the subject the procedure is the same, except that no means of retention are necessary.

Imprimis, it is necessary to know the relation of temperature in the medulla oblongata to that in the rectum. The following experiments show that the temperatures are the same:

Rabbit P trephined and inoculated June 9th, 1898, 9 a. m. 10.30 a. m., put in hot-air chamber (185° F.) for ten minutes. Rabbit came out dead and drawn up stiffly. Temperature before going into hot air, 104° F. Thermometer in case, after coming out of hot air, 113° + F. (thermometer registers no higher). Temperature in rectum after death, 113° F.; in medulla oblongata after death, 113° F. Atmospheric temperature, maximum, 89°; minimum, 69°.

Rabbit Q, trephined June 9th, 1898, 9 a. m., suffers some trauma, turns around from right to left; was with rabbit P in same basket in hot room, in temperature 185° F. for ten minutes; escaped from basket and jumped sideways about hot-air room. (This apartment is the hot-air room of a bathing establishment two blocks distant from this laboratory.)

Temperature before going into hot air, 103° F. Thermometer broken in case is higher than mercury registers, 113° + F. Fifteen minutes after return, temperature in rectum is 112.2° F.; in medulla oblongata, 112.2° F. Atmosphere: maximum, 89° F.; minimum, 69° F.

To get the temperature in the medulla oblongata, rapidly tear off the calvarium and thrust the thermometer through brain into spinal canal; the procedure is easy.

The result of the experiment on rabbits P and Q shows that the temperatures in the rectum and in the medulla oblongata correspond.

Rabbit A was trephined and inoculated with fixed virus, 159 removes, May 9th, 1898, 9 a. m. May 10th, 10.20 a. m., put in hot-air room, temperature 162° F., for 15 minutes. May 11th, 10.20 a. m., in 161° F. for 15 minutes. May 12th, 160° F. for 15 minutes.

"Man at this temperature for 15 minutes, especially if stomach is out of order, may have headache and flushing of face; he should then go out and apply cold water to the feet. Man can endure about 115° F. moist heat for about ten minutes." Practical non-scientific opinion.

Control rabbit in same room, same basket,

same temperature (not inoculated). Temperature before, 102.3° F.; after (thermometer in case in rectum), 105.9° F. Sweating freely around muzzle.

May 13th: Rabbit A in 175° F. for ten minutes. Control rabbit (not inoculated), otherwise same condition. Temperature before, 102° F.; after (thermometer in case in rectum), 110° F.—all its graduation.

May 14th: Rabbit A in 175° F. for 12 minutes; tremulous when it returned, 11 a. m. Found dead 3 p. m.

Two rabbits were trephined from medulla oblongata of A. One developed typical rabies in six days and died of it. The other took no disease, accidentally escaped. The virus in medulla oblongata of A was not sterilized or attenuated by temperatures of 106° F. and 110° F. The mercury rose to what would have been 111° F. if graduated. Medulla oblongata of A was virulent on the sixth day.

Rabbit C trephined and inoculated with fixed virus, 152 removes, on May 10th, 1898, 9 a. m. May 15th, 10 a. m., in hot air, 180° F., for 15 minutes. Rabbit dead when it came back. Temperature before 104.5° F.; after (thermometer

out of case), 109° F. Thermometer in case had slipped out and of course its registration is disregarded. Control rabbit not trephined, otherwise condition identical. Temperature before, 103.2° F.; after (thermometer in case in rectum), 109.9° F. Twenty-five minutes after return temperature in rectum, 107.8° F. Sweats around muzzle, panting respiration, but rapidly recovers. This is a dangerous temperature.

Two rabbits trephined from C both developed rabies in six days and died of it. Therefore the virus in the medulla oblongata of rabbit C was not attenuated or sterilized by a single exposure of the rabbit to 180° F. for 15 minutes. On the sixth day after inoculation temperature in medulla oblongata assumed to be 109° F.

Rabbit D, trephined and inoculated May 15th, 1898, 12 m.

May 16th, 10.20 a. m.: In hot air, 160° F., for 15 minutes. Temperature before, 102.8° F.; after (thermometer in case in rectum), 105.2° F. May 17th: In 160° F. for ten minutes. Temperature before, 102.8° F.; after (thermometer in case in rectum), 104.4° F. May 18th: In 160° F. for ten minutes. Temperature before, 102.2° F.; after (thermometer in case in rec-

tum), 104° F. May 19th: In 160° F. for 15 minutes. Temperature before, 102.4° F.; after (thermometer in case in rectum), 105.4° F. May 20th: Same temperature, 102.8° F. before, 106.4° F. after. May 21st: Same temperature, 104.2° F. before, 107° F. after rabic rise of temperature. May 22d: Same temperature, 104.4° F. before, 106.8° F. after. Slight gritting of teeth. May 23d: Same temperature, 105.4° F. before, 107.2° F. after. May 24th: Same temperature, 103.5° F. before, 104.8° F. after. Cannot stand up. Falls over and over. Paralytic rabies. May 25th: Same temperature, 100.7° F. before, 102.7° F. after rabic fall of temperature. May 26th: Same temperature before, 96° F.; after, 96.4° F. May 27th: Same temperature. No registration. Returned dead.

Therefore an average temperature of 104° F. in the medulla oblongata begun 22 hours after inoculation and daily repeated for 12 days, fails to sterilize or attenuate the virus in the medulla oblongata of the living animal (rabbit).

Rabbit R, trephined June 10th, 1898, 9.30 a. m. At 10.30 a. m., one hour after, was submitted to 185° F. for five minutes. Temperature before, 102.2° F.; after, 105° F.

		Temperature	
		Before.	After.
June 11th, 185°F.	for 5 minutes.	102.8°F.	103.2°F.
June 12th, 180	for 5 minutes.	103	105.8
June 13th, 180	for 5 minutes.	101.6	104.4
June 14th, 150	for 15 minutes.	104.4	108.6
June 15th, 158	for 15 minutes.	104.2	108
June 16th, 180	for 5 minutes.	404.8 (Rabic rise.)	106

At 11 a. m. this rabbit runs about room without evident disorder of motility; 4 p. m. it oscillates slightly.

		Temperature	
		Before.	After.
June 17th, 180°F.	for 6 minutes.	105°F.	105.6°F.
June 18th, 180	for 5 minutes.	105	105.2

Very incoördinate.

		Temperature	
		Before.	After.
June 19th, 180°F.	for 5 minutes.	103.6°F.	106.5°F.
June 20th, 180	for 5 minutes.	104.5	105
June 21st, 180	for 5 minutes.	100.2 (Rabic fall.)	101.4

June 22d, dying. Died on June 24th.

A rabbit one hour after inoculation, subdurally, is daily submitted to temperature of over 104° F. in medulla oblongata on an average, twice 108° F., twice 106° F., four times 105° F., yet it takes rabies after the usual incubation and dies of it. The virus in the medulla oblongata of this living rabbit has not been sterilized or attenuated.

Rabbit S was trephined and inoculated with fixed virus, 154 removes, on June 10th, 9.30 a. m. At 10.30 it was subjected to hot air as follows:

		Temperature	
		Before.	After.
June 10th,	185°F. for 5 minutes.	104.8°F.	107°F.
June 11th,	185 for 5 minutes.	102.8	102.6
June 12th,	180 for 5 minutes.	103.4	106
June 13th,	180 for 5 minutes.	103.8	105
June 14th,	150 for 15 minutes.	103.8	106
June 15th,	158 for 15 minutes.	103.4	107
June 16th,	180 for 5 minutes.	103.6	104

Six days after inoculation: 10.20 a. m., no impairment of motility; 4 p. m., head slightly but decidedly awry.

		Temperature	
		Before.	After.
June 17th,	180°F. for 6 minutes.	105.2°F.	106°F.
June 18th,	180 for 5 minutes.	101.4 (Rabic fall.)	102
June 19th,	180 for 5 minutes.	96.6	99
June 20th, found dead 10 a. m.			

A rabbit with temperature over 104° F. daily for five minutes (twice 107° F., three times 106° F.) fails to attenuate or sterilize the virus in the medulla oblongata.

A vigorous man, aged 24 years, weight 140 pounds, with the thermometer in the case and in rectum entering within anus, subjected himself, June 22d, 1898 (atmospheric temperature, 77°

F., 11 a. m.), to temperature of 162° F. dry air for 15 minutes. Temperature before, 98.4° F.; after, 101.2° F.

June 25th, 1898, 4 p. m.: Atmospheric temperature, 94° F. Subjected to temperature 180° F. for five minutes; before, 98.4° F.; after, 106.2° F. Cold douche and cold-water swimming in 30 minutes reduced temperature to 98.2° F. While subject to 180° F. dry air, he became dizzy, and "things looked blue"; the floor tiling burned the soles of his feet and he walked on his heels to relieve the more sensitive part.

Is it possible to maintain a temperature of 104° F. in the human medulla oblongata for eight days? And if so, would it cure or prevent rabies? We have answered the second part of this question negatively. With a temperature of 108° F. it does attenuate, and finally sterilizes the virus, but too late to prevent the disease. To all of which it may be objected that inoculation, subdurally, at once imparts the virus to the nervous system, and that bites as they occur in nature should be more closely imitated, *e. g.*, by hypodermic injection of virus. In making which experiment, its frequent failure to cause the disease must be taken into account.

The writer makes no claim to originality in this paper, except in the sections on septicæmia, rabies in the mouse, Baltimore cases, and others, and in the experiment relating to the effect of heat; in the conduct of which he acknowledges his obligation to Mr. Melcher Ekstromer; and to Mr. Philip S. Chancellor for translations.

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RABIES.

Supplementary Article.

PATHOLOGY.

The morbid histology of the nerve ganglia in rabies has received recent investigation (1889-1900) which has evoked discussion and contention. Van Gehuchten and Nelis maintain that these lesions are of paramount importance; Babes, while admitting their existence, deems them less manifest than those of the brain and cord.

On section of a ganglion we find angular or ovoidal nerve cells, each cell situated in a somewhat circular space, which is bordered with connective-tissue corpuscles. The surrounding tissue is slightly fibrillated, with its corpuscles not very numerous. In rabies the corpuscles around the nerve spaces become detached; there is also a hyperplasia of connective-tissue corpuscles, especially marked at the boundary of the ganglion. The size of the cells and corpuscles varies according to the animal from which they are derived. In the dog, man, and rabbit the

corpuscles are so large that they have been designated epithelioid and embryonic; in the cat and pig they are so small as to resemble leucocytes under moderate magnification. This cell hyperproliferation is sometimes so excessive as to form in spots microscopic nodules, suggestive of analogy to lepra or other infective granulomata (Nelis). This over-production of corpuscles may be all that is observed if the animal has been killed after having been sick for a not very long time; if very early killed there may be little or no change; when permitted to die, the appearances are more graphic; the cells also become involved, some being pallid, faintly granular, and much enlarged. Their protoplasm is vacuolated and the cell contour may present crescentic or hemispherical scallops. The nucleus may be displaced or extruded, it becomes indistinct, and in an occasional cell it undergoes degenerative proliferation, forming a coarsely granular mass or somewhat rosette-shaped figures, or it may become pale, enlarged, distinctly circular, sharply outlined, and pigmented; in this latter form it is sometimes found outside the nerve cell in the tissue. Finally, the nerve cells, in greater or less numbers, become destroyed and disappear, leav-

ing vacant spaces. Alongside the blood-vessels there is often very decided leucocytic extravasation.

Van Gehuchten accredits Nepveu with priority in discovery of these lesions; remarking that he (Nepveu) "did not attach the least importance to these investigations"; subsequent investigators have attached too much importance to them. In 1872 Polaillon and Nepveu noted characteristic lesions in a man dead of rabies. The whole cerebrospinal axis was the seat of a strong congestion. The ganglion of Gasser was not excepted from that hyperæmic state; it was infiltrated with round or oval cells. "These cells were found in large numbers around the ganglion cells, 12 or 16 and sometimes more. Some among these cells have a hyaline aspect and are probably epithelioid cells of the capsule of the ganglion cells." The presence of these cells had modified the aspect of the nerve cells, which were jagged, irregular, shrunken, and also deprived of coloring matter. In some rare spots the white cells were aggregated in a focus (J. Crocq). These investigations remained for 28 years a dead letter (Babes). Then Van Gehuchten and Nelis revived, elaborated, and

laid stress upon them (1889, 1890). "It is in the peripheral nerve ganglia, the cerebro-spinal, and sympathetic, that the rabic virus exercises, by preference, its deleterious action. Rabies seems to us to be a specific affection of the peripheral neuron of sensation. The rabid animal is paralyzed because it is insensitive." The lack of muscular sense may explain its incoördination. Babes asserts: "I have had occasion to study two cases of rabies in man, in both the sensibility, carefully examined in the paralyzed parts, was intact." Babes in 1892 remarks, not, however, referring to the ganglia: "That which above all characterizes the lesion is the presence of the pericellular nodules—the collection of cells about the nerve cells, which has been termed the rabic tubercle."

Van Gehuchten and Nelis claim that the rabic tubercles of Babes have not the importance attributed to them by that investigator. "They did not exist in our two cases of human rabies. Babes himself affirms that they are in default in animals inoculated with the fixed virus. The lesions described up to the present are not then of a character sufficiently specific to enable them to be useful as an element of diagnosis." The

foregoing observations are made by Van Gehuchten and Nelis regarding the researches of others, especially of Babes.

Van Gehuchten further states: "It is necessary to examine the ganglia of the dog dead of natural rabies. M. Crocq forgets that if, in rabies determined experimentally by the fixed virus, the ganglionic lesions are wanting, so also are the vascular and cellular lesions, as Babes has shown a long time since." Therefore, so far as the fixed virus is concerned, the revelations of Van Gehuchten, Nelis, and Babes are all equally at fault. Evidently the fixed virus should exhibit the essential lesions of rabies. All other lesions must be non-essential, attributable to concomitant, not causal organisms. Most typical rabies may then exist according to Babes, Van Gehuchten, and Nelis, with the lesions described by them eliminated, thus proving that they are non-essential. Admitting the fact, it is impossible to escape the logically demonstrated conclusion which deprives the lesions in question of the slightest claim to specificity. "The street virus and the fixed virus must present profound differences between themselves, and as the fixed virus comes from the street virus, one must

admit that its mode of action upon the organism arises insensibly during its passage from one animal to another" (Van Gehuchten and Nelis). This is an explanation which does not explain. In point of fact, rabbits dead of the fixed virus subdurally inoculated do exhibit in their ganglia the lesions in question. They may not all do so, many may not do so; but if any do, it is sufficient to prove the affirmative assertion. There are in my possession ganglia of rabbits of the five hundred and seventy-third passage (Paris virus), and of the two hundred and sixty-seventh passage (virus introduced by the writer, starting from the medulla oblongata of a rabid cow); these ganglia present exquisitely the morbid morphology of rabies, which has been erroneously supposed to be restricted to animals dead of the street virus. Golgi, using a fixed virus, makes the following observations, which exactly apply to the condition of the ganglia above referred to: "I have always found the intervertebral ganglia changed; although these changes were inconstantly localized in the different groups, the entire picture was absolutely characteristic. Besides the well-known round-cell accumulation and vascular dilatation which

have often been spoken of, I want to emphasize especially the vacuole formation, which takes place to such extent as to give the cell a cyst-like appearance; further, the coarsely granular condition of the cell protoplasm, which chiefly takes place in the centre, being surrounded by a peripheral homogeneous zone; then the displacement of the nucleus toward the periphery, the nucleus at the same time appearing elongated, gives the impression as if it had been compressed. The nucleus is often found at the extreme edge of the cell, where it might be very easily overlooked; in a few cases it is found outside the cell under the cell membrane. The peripheral homogeneous zone is most often found in the cells, which show a coarsely granular interior, and in these cells the nucleus is occasionally formed by an accumulation of chromatic particles in a condition of advanced regressive metamorphosis."

In an article entitled " Les Lésions Anatomo-Pathologiques de la Rage sont elles spécifiques," J. Crocq concludes:

" 1. Neither the vascular nor the cellular lesions described by authors anterior to Van Gehuchten, nor the capsular lesions of that author

are, properly speaking, specific of rabies. The first are only manifestations of an inflammation and of a profound infection of the nervous centres; the second appear to be the result of special conditions, in which organisms profoundly intoxicant are found.

" 2. The anatomo-pathological lesions of rabies actually known may be encountered in other maladies.

" 3. Rabies consists in a toxic infection very acute, provoking profound alterations, chemical and physical, without proper specificity, in the nerve axis, and in the peripheric ganglia.

" 4. The pathological physiology of rabies explains itself relatively easily by lesions vascular, cellular, pericellular, and chemical, extending themselves to the whole nervous system, central and peripheral.

" 5. The aspect of the ganglion knot of the vagus in animals dead of street rabies (rage des rues) is so special, so characteristic, that the microscopical examination of this ganglion actually remains the method most simple and most sure to establish the diagnosis of rabies in the dog which bites.

" 6. If the ascertaining of that lesion permits

us to affirm probably rabies in the dog which bites, its absence does not suffice to exclude in a manner absolutely decisive the rabic infection."

M. Cornil asseverates: "The examination of nerve ganglia at this point of view is most difficult. For a long time the normal conjunctive (lymph?) path has been taken for a lesion. As to the cellular lesions it is only recently that they have been studied, thanks to the progress of technique."

Prof. Henry J. Berkley, of Johns Hopkins University, and Prof. Camille Golgi, of the University of Pavia, are the chief exponents of the advanced technique as regards rabies. Berkley's work is restricted to the cerebral and cerebellar cortex; Golgi's researches include also the ganglia. These authorities are not in accord, though their differences are not irreconcilable. Both used a fixed virus. Berkley finds a paucity of lesions and generalized; Golgi, an abundance and localized.

Berkley failed to find any evidence of coarse lesions of the vessels in the form of extensive hyperæmias, plastic exudates, and extensive emigration of corpuscular elements into the perivascular sheaths, nor could a single extravasa-

tion of the red blood corpuscles be found as has been described by Popoff and others in the human subject (this must have been infection with street virus). "The sheaths of the vessels are not greatly altered, the endothelial nuclei are not swollen, some of the nuclei of the muscularis show a tendency to absorb less of the aniline stain than usual and show vacuoles, but the muscular fibres are not swollen or hyaline, and altogether the evidence of a degenerative process taking place in the walls of the nutrient vessels is inconsiderable.

"We have, therefore, in the present cases only the indications of a mild infection, of a sufficient intensity, it is true, to cause death after the lapse of a considerable number of days, but insufficient to cause any considerable morbid change of the vascular walls, together with a degree of leucocytosis such as is often found when the soluble poison of bacterial source acts with a considerable degree of energy upon the blood-forming organs.

"These conditions are therefore most favorable to enable one to ascertain the effect of the subtle poison from the rabies bacterium upon the nerve elements. Golgi's cases, in which he

found karyomitoses of the nuclei of the vascular muscles, must have been of greater severity, and the damage to the nutrient supply have borne its part in the production of the nerve cell changes which we are now able to exclude to a certain degree.

"*Alteration in the Nerve Elements Found in the Nissl Preparations.*—Interest in the stichochromic cells of the cortex centres not in the protoplasm, where indeed alterations are ill defined, but in the contents of the central vesicle. In the place of the clear vesicle holding a nucleus and a variable number of adnucleolar particles in a clear karyoplasm, we have now its contents everywhere turbid and more deeply stained than normal, the nucleolar particles showing a variety of dispositions. They are roughened and much larger than ordinary, so much so that the actual nucleolus is no longer distinguishable from them. These particles are either scattered equally through the karyoplasm, or are segregated toward the central nuclear point and form figures similar to those found in chronic alcoholism, though less pronounced, as the extreme degree of roughness is no longer seen. Very few nuclei can be discerned showing the normal disposition

of the chromatin particles. In a few of the largest pyramidal cells where the lesions of the nuclei are not far advanced and the nucleolus can be determined, it has the appearance of being empty of all contents, the central portion remaining unstained, with a surrounding deeply dyed membrane, from which numerous projections pass an infinitesimal distance toward its centre. Vacuolation of nuclei was also seen by Popoff, who figures a certain roughness of the nucleolar particles, less pronounced than in the present instances.

"*Changes in the Nerve Elements Seen with the Silver Phosphomolybdate Method.*—The lesions of the cortical cells in hydrophobia, as seen with this method, are on the same order as those induced by other irritants to the tissues of the region, but present some slight differences from those we have already studied. The distribution of the pathological changes is very widespread among the cortical cells, which are no longer present in groups and certain regions of the cellular layers, as is the rule with some of the weaker toxins. Everywhere in a section the dendrites of the cells are found to be involved in the degeneration, and it is rare to see a cell

in which all the various branches have been completely spared. The tumefactions are frequent along the stems, but are all of small size; and the portions of the dendrite intervening between the swellings are thin and have but very few of the gemmules still adherent to them, and of these remaining still fewer show perfect staining. On the swellings the lateral buds have completely disappeared, and left no trace of their former presence. A very careful search had to be made to discover any completely normal cells among the diseased ones.

"But few of the corpora show distinct implication in the process of degeneration. An occasional one may be found having some erosion of its body, but these are rare. Lesions of the neuraxon in the form of beaded swellings, such as Golgi has described, appear to be infrequent, for in the series of several hundred preparations not more than half a dozen such cylinders could be found.

"Neuroglia alterations are likewise not definite. There is certainly no multiplication of either the star-rayed neuroglia or the vascular cells; the latter may now and then show bodies and virus that may possibly be a little tumefied,

but it is hardly sufficient to enable one to state that it is a distinct alteration. Golgi figures granular, fatty degeneration of the neuroglia cells diffusely scattered through the entire nervous system.

" The branches of the Purkinje cells show a small percentage of swellings. Some of the knots are of considerable size and are well stained. The lateral buds are retained in part upon these swellings, while otherwise the branches show no diminution of the protoplasmic fur, in strong contrast to the projection cells of the cerebrum, evidencing that they are capable of greater resistance to the effects of this, as well as other poisons, than the cerebral elements. The other nerve elements of the cerebellum are not sufficiently frequently stained to permit one to determine with certainty whether they are abnormal or not. The neuroglia elements have the same conditions apparent in them as in the corresponding elements of the hemispheres.

" This investigation departs in a number of particulars in its results from the one by Golgi. We find the degenerated cells universally present in every portion of the cortex, while he sees them only freely distributed. More important

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is the supposed primary involvement of the nerve cell and afterward the dendrites to their terminations. This is entirely contrary to the results obtained in any of those studies on the action of poisons on the nerve cells (alcohol, serum, ricin), and it is against the law of degeneration of the nerve cells for the element to die from its centre outwardly; either the lesion begins at the periphery and extends centralward, or all the component members of the cells undergo necrosis synchronously. Golgi makes no mention of the condition of the gemmules on the dendrons in these atrophic conditions. It is extremely probable that his stain failed to color them at all, otherwise it is hardly possible that he should have overlooked such an important and readily distinguishable feature of cell degeneration as their shedding represents.

"While it is true that the same swelling of the axis-cylinder fibre was found in this study as had been previously described, the lesion must be held to be a rare one, and not of sufficient frequency to constitute one of importance.

"I can see no signs of anything approaching an inflammatory process taking place in the cerebral tissues, only the indications of a purely de-

generative reaction from the effect of the toxic substance produced by the bacterium of hydrophobia, essentially causing the same pathological changes as those induced by other soluble poisons when present in the circulation in sufficient quantity to disturb tissue nutrition."

The investigations of Berkley are quoted thus in detail because they set forth the essential lesion of rabies in the structures examined.

Inflammation consists of a group of features; it is impossible to designate the essential one. A feature may be pointed out as absolutely indicative of inflammation, *e. g.*, pus or fibrin formation, but inflammation may exist without these features. It may be too restrictive to assert that leucocytic extravasation is the essence of inflammation; a degenerating vessel wall may permit this. It is certain that in rabies leucocytic and erythrocytic extravasation does occur. If the definition of inflammation be, some effect on the vessel wall allowing corpuscular extravasation, then Babes and others, referring to microscopic lesions in the nervous system as inflammatory, are entirely correct. It is certain that the coarse lesions of inflammation are not found in rabies as in infectious diseases and septicæmias. There

are no coarse lesions of meningitis, myelitis, peri- or endocarditis, pleuritis, pneumonitis, peritonitis, so common as effects of phlogistic bacteria.

It may be regarded as axiomatic that histogenesis exhibits the same morbid morphology in absolutely diverse diseases; there may be a varietal distinction, for the most part finely microscopic and difficult of detection.

ETIOLOGY.

In relation to the as yet (1902) undiscovered cause of rabies, the researches of Bruschettini are interesting. The following is extracted from "La Rage" by Dr. Auguste Marie: "Starting with the idea that the microbe of rabies required for its development the nerve chemical products, the author prepared a jelly adding lecithin from the yolk of eggs or cerebrin extracted from the brain of the dog or rabbit. Upon agar tubes were sown particles of the bulb (medulla oblongata) of a rabbit killed by the fixed virus. After 24 or 36 hours' sojourn in the oven, confluent colonies appeared, very small, transparent, and difficult to see with the naked eye, resembling little drops of water. These were dispersed

lightly on the surface of the jelly; it is easy to resow and to obtain successive generations. By a strong enlargement these colonies appear irregularly dentated along the border, with a dark zone in the centre. These colonies consist of bacilli, short, very small, thick-set. They color easily with Ziehl and the blue of Loeffler. The staining causes to appear at the centre of the microbe a clear zone as in the diplococcus of Fraenkel. In liquids, such as bouillon of brain with the addition of glucose and glycerin, coccal forms are seen to develop which in old cultures are colored violet-red by the Loeffler blue. The microbe grows well at 16° C. (60.8° F.). Its development is slowed in vacuo; it is non-motile.

"The subdural injection of these cultures killed rabbits in from five to eight days, with all the signs of rabic paralysis, and the inoculated medulla transmitted rabies in series. Finally, the microbe was found in sections of the nerve centres in the rabid animals and in those which had succumbed to the injection of the bacillus of Bruschettini.

"The experiments of Bruschettini were repeated at the Institut Pasteur. There it was found that the nerve centres of rabid rabbits

presented a microbe responding to the description which we have given. This bacillus was easily cultivated in the media indicated, and its culture provoked in rabbits the phenomena of paraplegia. And yet this microbe is not that of rabies because it is found (with a little less frequency, it is true) in the nerve centres of rabbits not rabid; moreover, inoculation of the dog with the microbe has not been known to provoke furious rabies. Finally, we cannot succeed in rendering refractory to rabies the animals inoculated with the culture of that bacillus."

It may be conjectured that such an organism as this, or one analogous to it, may have caused the general paralysis, recorded as having occurred in three persons under treatment.

DIAGNOSIS.

The outcome of the pathology should be the diagnosis, but there is a conflict of opinion regarding the interpretation of this morbid histology. Microscopic appearances closely resembling, if not identical with, those found in rabies are present in many totally different diseases, especially in uræmic and septicæmic conditions. Babes asserts that the lesions of tetanus above

all closely resemble those of rabies; so also do those of puerperal eclampsia (nephritic), but the small cells are not evidently connected with the vessels, nor are they more disposed around the nerve cells. The morbid histology is essentially the same whether in brain, spinal cord, or ganglion, except that in the latter the normal cells, being arranged in capsules lined with endothelial cells, give a different varietal morphology to this lesion.

Babes, while admitting that the lesions of rabies have nothing absolutely characteristic, and that in a marked case of diffused myelitis one might find similar lesions, says: "It must nevertheless be admitted that neither in books nor in my personal experience have I ever met a case similar; therefore up to the present (1900) we may regard rabies as characteristic." To assure himself of the specificity of the lesions found in rabies, Babes examined a considerable number of specimens from dogs and men dead of acute affections of the nerve centres. He observed sometimes vascular lesions much more intense and foci much more extensive than in rabies, but he did not find the embryonic foci around the nerve cells. On this last point Babes fixes the

diagnosis. Future observations will probably show that it is not restricted to rabies, in which it is not always present. Referring to ganglionic lesions he (Babes) depreciates their diagnostic value in the following remarks (with which the writer inclines to agree):

"In my memoirs on the pathology of the spinal ganglia I have described similar lesions in many diseases, and I have insisted upon the difficulty of appreciation of lesions less grave because of the varied aspect of the normal ganglion cells, which often are found to be discolored (decolorized), and also without nuclei in normal ganglia. Moreover, the chromatic elements of the cells are of different types and more difficult to appreciate than in the large cells of the cord. Finally the nuclei of the ganglion cells are sometimes displaced in the normal state; also the number of cells bordering the elements (nerve cells) multiply themselves with facility as a result of different irritations."

These ganglionic lesions are often present in rabies and not seldom in other diseases, which, however, with the exception of septicæmia and tetanus are not common in the lower animals; especially is the latter uncommon in dogs. In

human beings I have observed the ganglionic changes in trauma of the spinal cord due to fracture of the vertebra, in tetanus, in malignant scarlet fever, and in diphtheria, in both of which death was caused by septicæmic infection; also in electrical death when not instantaneous, and in a case of pleuropneumonia in a dog.

The large proportion of suspected animals that do have rabies is remarkable. In 157 cases, nearly all dogs, tested by subdural inoculation of rabbits, there were only four which did not develop rabies. In 31 cases in which ganglia were examined and positive lesions found, there were three cases, dogs, from which the rabbits subdurally inoculated did not develop the disease; one cat and one pig gave positive results.

The large majority of authorities assent to the following propositions of M. Hebrant: "The value of this positive lesion seems to us at the present time (1900) sufficiently established. Therefore, in our opinion, it is possible to advance the following conclusion: Whenever in a suspected dog (or, of course, other animal) the microscopic examination of the ganglia allows us to see the lesions pointed out by MM. Nelis and Van Gehuchten, it must be declared

that the animal is positively mad. The ganglionic lesions noted by Van Gehuchten and Nelis in street rabies are not constant. The absence of the lesions does not permit us to exclude in a decisive manner rabic infection."

The pathological diagnosis, in itself so interesting and instructive, has no bearing upon the practical question of treatment. If the result is negative, it does not exclude rabies; if positive, the patient is to be treated. Under these circumstances the patient must be treated anyhow, irrespective of the pathology. Furthermore, it is inadvisable to communicate the pathological results to those concerned, because the final, demonstrative confirmation depends upon animal experimentation. If from a suspected animal other animals be experimentally infected with rabies, and rabies be passed from these to another series, it permits us to affirm, beyond the possibility of doubt, the presence of rabies in the suspected animal. Though an affirmative diagnosis of rabies can thus certainly be made experimentally, a negative diagnosis cannot be made in the same way. The absence of rabies in the suspected animal is that which those bitten most ardently desire to know. In either case the

experimental result approximates certainty much closer than the findings or non-findings of pathological investigation.

The operator who makes the experiment should be skilful. He trephines and inoculates subdurally four rabbits, one on each of four successive days, or two on each of two successive days; between the operations the medulla oblongata, portions of which are inoculated, should be kept in sterile test tubes on ice, and if at all decomposed, it should be immersed in neutral glycerin. Should these rabbits fail to develop rabies at the usual time, 12 or 15 days after the operation, and if, at the expiration of three months, they are still well, unless the virus in the medulla oblongata has been destroyed, the animal in question did not have the virus in its medulla oblongata; in fact, it did not have rabies. The rabic virus resists freezing and putrefaction. It is sterilized at once by a temperature of 118° F. and slowly by one of 108° F. A hot glass rod used in rubbing up the medulla oblongata in water may attenuate or even sterilize the virus; but an experienced operator would not so blunder. Animal experimentation does affirmatively prove the existence of rabies

with absolute certainty; it negatives the existence of rabies as certainly as negative evidence can. The microscope does not enable us to arrive at a negative diagnosis; affirmatively it only raises a probability of the presence of rabies. It affords no sure basis for rapid diagnosis of rabies; it is a conjectural diagnosis, contingent upon the absence of numerous disorders.

The following are actual examples of the practical application of ganglionic diagnosis: A bitten person (the ganglionic pathology being present) was assured that the dog was rabid, but later on, the rabbit subdurally inoculated failing to develop, it became necessary to reassure the patient that the dog was not rabid. This was an awkward situation for the doctor, but involved no more serious consequence than loss of confidence. Advice along this line has, however, involved loss of life. Two patients were informed that the ganglia of the dog did not show rabies; it was explained to them that this did not prove the disease absent. They decided to await the result of the experiment, which showed that it was rabies; it was then too late to save these lives. Nothing should have been said to these persons. They should have been simply

told that treatment was urgently necessary. " No doubtful balance of rights and wrongs " should be submitted to the average human mind which cannot digest the *pro* and *con* of abstruse data.

Diphtheria clinically and experimentally may give rise to symptoms closely resembling rabies. Such cases, especially if the persons have been bitten by a supposed rabid animal, may be mistaken for rabies. It is well known that the bacillus diphtheriæ may be found in various organs and in the nervous system, medulla oblongata, ventricles, etc. A very interesting case of this kind is reported by Drs. Head and Wilson, of the University of Minnesota. In about 65 days after having been bitten on the left cheek by a dog, a lady developed the signs of rabies; especially the spasm and difficulty in swallowing water. She died in about 11 days. Rabbits subdurally inoculated from her medulla developed, and died with symptoms of, rabies. In the nervous system of the dead woman and in the rabbits the bacillus diphtheriæ was found. Rabbits hypodermically injected with diphtheria antitoxin and afterward injected subdurally with the supposed rabic medulla oblongata escaped

infection. The diphtheria antitoxin does not protect against rabic inoculation.

The writer injected subdurally a hen with the egg of another that had died of rabies. After a prolonged incubation the subject of this experiment developed a paralysis like that of rabies. Opening by chance its beak, the mouth and throat were seen to be full of diphtheritic membrane. Of course the paralysis was diphtheritic.

TREATMENT.

In order to determine the value of treatment it is necessary to know the natural history of the disease; how the disease behaves when not treated at all. Of persons bitten by rabid dogs, how many develop rabies when not treated? From 1850 to 1872, which period antedates the Pasteur treatment, an annual average of 30 persons died of rabies in France; during the above period (22 years) 660 persons died of this disease. Contrast with this the statistics of the Institut Pasteur, Paris, which show that from 1886 to 1896, inclusive, of 2,730 persons bitten by animals experimentally proven rabid only 19

died of the disease; also the following tabulation from the same years:

	Cases.	Died.	Mortality (per cent.)
A	2,730	19	0.69
B	11,629	56	.48
C	4,286	15	.35
	18,645	90	0.48

Table A includes cases in which the biting animal was experimentally demonstrated rabid.

Table B includes cases in which the biting animal was certified rabid by examination of a veterinarian.

Table C animals suspected to be rabid.

	Cases.	Died.	Mortality (per cent.)
Bitten on the head	1,608	21	1.36
Bitten on the hands	10,254	49	.47
Bitten on the limbs	6,783	20	.29
	18,645	90	0.48

The schools of Alfort, of Toulouse, of Lyons, of Berlin, give one-quarter or even one-third as the proportion that take rabies after having received infected bites, which accords with the experimental results of Hertwig, who

produced rabies six times in 16 subcutaneous inoculations, and of Renaut, who in 166 injections beneath the skin obtained 67 positive results. The seat of the injections and the animals used should be stated. Deep injections in the cervical region cause rabies much more frequently than those into the back or belly. Using the latter sites, the writer subcutaneously injecting guinea-pigs had only one successful case in 16. Difference in locality might explain the disagreement with Hertwig's result, who may have deeply injected the neck. In the experiment the insertion of a definite quantity of virus is insured, which is not always so in bites as they naturally occur, especially in those through clothing. At first view experimental inoculations seem to be more sure to give positive results and therefore more dangerous; but further consideration shows that the situation, the multiplicity, and the character of the natural inoculations (bites) must be given due importance in estimating their gravity.

How many bitten by dogs demonstrated rabid escape when not treated? Previous to the Pasteur epoch (1885) there was no accurate method of demonstration; subsequent to this period very few of those bitten by suspected dogs remain un-

treated. The diagnosis of rabies, independent of experimental demonstration, is seldom wrong. What percentage of those bitten by dogs suspected to be rabid develop the disease? The estimate of 5 per cent., ascribed to John Hunter, is the "*pièce de résistance*" of those who discredit the Pasteur treatment. This percentage may in the ordinary run of bites be accepted as correct; but assorted statistics, based on the site, number, and character of these wounds very much raise the estimate. Severe and multiple bites on the head, face, and neck when untreated will give more than 50 per cent. mortality. The John Hunter figures show that five out of 100 bitten by rabid dogs die if not treated. It is not pleasant to be in a category of 100 of which five are due to die of rabies in 90 days more or less. The Pasteur Institute figures show that better things are in store for those treated. Of 2,730 bitten by dogs demonstrated mad 19 died (0.69 + per cent.), less than half the annual death rate of Baltimore City, which is 1.74 per cent. "If with Högyes one recapitulates the average of mortality established in 24 antirabic laboratories, it is found that of 54,620 persons treated 423 died, which gives about 0.77 per

cent. It is well to remark that in several of these institutions many wolf bites are treated, which are very dangerous because of their seat, multiplicity, and depth. It must be admitted, on the other hand, that many of the individuals treated may not have been bitten by rabid animals." The first of the following tables is arranged in the categories A, B, C; the second according to the gravity of the infected bites, as indicated by their situation. The tables are from "La Rage" (Marie), who quotes them from Högyes.

Some of the subjoined tables set forth the results of treatment, which offer as reliable reasons for action as are attainable in the ordinary transactions of daily life.

FIRST TABLE.—CLASSES A, B, C.

Antirabic institutions.	Years.	Classes A and B.			Class C.		
		Persons treated.	Deaths.	Mortality (per cent.)	Persons treated.	Deaths.	Mortality (per cent.)
Paris	1886–1895	13,429	71	0.52	3,840	12	0.36
Naples.....	1886–1895	980	10	1.03	289	2	.69
Turin	1886–1894	1,926	21	1.09	281	0	.00
Totals....	.....	16,335	102	0.62	4,410	14	0.31

SECOND TABLE.—ACCORDING TO THE SERIOUSNESS OF BITES.

Antirabic institutions.	Years.	Head and face.			Hands.			Feet, trunk, covered regions.			Totals.		
		Persons treated.	Deaths.	Mortality (per cent.)	Persons treated.	Deaths.	Mortality (per cent.)	Persons treated.	Deaths.	Mortality (per cent.)	Persons treated.	Deaths.	Mortality (per cent.)
Paris ...	1886–1895	1,503	19	1.26	9,551	48	0.50	6,283	16	0.25	17,337	83	0.47
Turin ..	1886–1894	169	6	3.54	1,260	14	1.11	778	1	.12	2,207	21	.95
Naples..	1886–1895	84	4	4.76	672	7	1.04	513	1	.19	1,269	12	.94
Pesth ...	1890–1895	479	24	5.01	1,983	22	1.10	2,452	13	.53	4,914	59	1.20
Totals		2,235	53	2.37	13,466	91	0.66	10,026	31	0.30	25,727	175	0.68
First treatment by dried cords.....		320	21	6.56	1,408	17	1.20	1,682	13	.77	3,410	51	1.49
Second treatment by dilutions		159	3	1.88	575	5	.86	770	13	.....	1,504	8	.53

The method of graduated virulent dilutions used by Högyes deserves notice. In cords dried over caustic potash (Pasteur method), the virulence does not always conform to their age; that is, cords which have been drying for a long time may be more virulent than those which have been drying for a shorter period, whereas the reverse should be the result. This variability is caused by the varying size of the cords; cords unequally thick dry themselves unequally, so that the virulence does not decrease uniformly and by regular degrees, according to the age of the cord. Högyes hoped to guard against these inconveniences by replacing the dried cords with a diluted fixed virus. He bases his views upon those of Pasteur, who asserts that desiccation in diminishing the virulence does not change the quality of the virus, but its quantity alone. Högyes takes 1 gm. of the bulb (medulla oblongata) of a rabbit that has died of the fixed virus. This is rubbed up as finely as possible, with the precautions of ordinary cleanliness, and very gradually to it is added liquid (*solution physiologique*) 0.6-per-cent. salt solution in the proportion of one part of nerve substance to 100 parts of the solution. The 1 :6,000 dilution

does not kill rabbits. The 1:5,000 dilution does not surely give rabies and the incubation is very long. The 1:10, 1:100 and 1:200 dilutions are as active as the most concentrated. The dilutions seem necessary in order to secure immunization. The result of treatment before and after infection varies. If the animal be treated before infection, it is protected in the majority of cases against every mode of inoculation of virus, the most intense trephining and subdural inoculation included. The treatment is of no avail when it follows an intracranial inoculation of fixed virus; also after the street virus similarly inoculated. Treatment practised in the trachea, subsequent to inoculation, prevents the disease one time out of five. It is entirely otherwise with bites and subcutaneous injections. Of eight dogs so treated not one contracted rabies, whereas of the eight control dogs bitten by the same animals five became sick of rabies, four died, and one was saved. Experiments in 70 dogs gave like results.

The following comparisons may be made between the virulence of dried cords and that of the dilutions. From the 1:10,000 up to the 1:6,000, the dilutions correspond to the series of cords from the fourteenth to the eighth day.

Injected under the dura mater they give rabies only exceptionally. The 1:5,000 dilution does not kill all the rabbits, or the sickness does not show itself until after a long incubation; it is equivalent to a seven-day dried cord. The 1:1,000, the 1:500, the 1:200 dilutions correspond to the sixth-, fifth-, fourth-day dried cords.

The virus is probably not equally distributed throughout the medulla oblongata. The fourth ventricle is supposed to be especially virulent, so that the better procedure might be to rub up the entire bulb and then take 1 gm. of this material. This method of Högyes is exact and the results of treatment are good.

BITES ON THE HEAD AND FACE.

Day of the inoculation.		Degree of the dilution.	Quantity in cubic centimeters.
First	morning..	$\frac{1}{10000} + \frac{1}{8000} + \frac{1}{6000}$	3 to 3 to 3
	evening ..	$\frac{1}{5000} + \frac{1}{2000}$	3 to 2
Second	morning..	$\frac{1}{5000} + \frac{1}{2000}$	3 to 2
	evening ..	$\frac{1}{1000} + \frac{1}{500}$	$1\frac{1}{2}$ to 1
Third	—morning..	$\frac{1}{200}$	1
Fourth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Fifth	morning..	$\frac{1}{1000} + \frac{1}{500}$	$1\frac{1}{2}$ to 1
	evening ..	$\frac{1}{200}$	1
Sixth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Seventh	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Eighth	—morning..	$\frac{1}{200}$	1
Ninth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Tenth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Eleventh	—morning..	$\frac{1}{200}$	1
Twelfth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Thirteenth	morning..	$\frac{1}{1000} + \frac{1}{500}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{200}$	1
Fourteenth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Fifteenth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Sixteenth	—morning..	$\frac{1}{200}$	1
Seventeenth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000} + \frac{1}{1000}$	2 to $1\frac{1}{2}$
Eighteenth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Nineteenth	—morning..	$\frac{1}{200}$	1
Twentieth	—morning..	$\frac{1}{100}$	1

BITES ON THE HANDS AND FEET.

Day of the inoculation.		Degree of the dilution.	Quantity in cubic centimeters.
First	morning..	$\frac{1}{10000} + \frac{1}{8000}$	3 to 3
	evening ..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
Second	morning..	$\frac{1}{5000}$	3
	evening ..	$\frac{1}{2000}$	2
Third	morning..	$\frac{1}{2000}$	2
	evening ..	$\frac{1}{1000}$	$1\frac{1}{2}$
Fourth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Fifth	—morning..	$\frac{1}{200}$	1
Sixth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000}$	2
Seventh	morning..	$\frac{1}{2000}$	2
	evening ..	$\frac{1}{1000}$	$1\frac{1}{2}$
Eighth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Ninth	—morning..	$\frac{1}{200}$	1
Tenth	morning..	$\frac{1}{6000} + \frac{1}{5000}$	3 to 3
	evening ..	$\frac{1}{2000}$	2
Eleventh	morning..	$\frac{1}{2000}$	2
	evening ..	$\frac{1}{1000}$	$1\frac{1}{2}$
Twelfth	morning..	$\frac{1}{1000}$	$1\frac{1}{2}$
	evening ..	$\frac{1}{500}$	1
Thirteenth	—morning..	$\frac{1}{200}$	1
Fourteenth	—morning..	$\frac{1}{100}$	1

As director of the Antirabic Department, College of Physicians and Surgeons, Baltimore City, Md., I have heretofore used the second table of the Pasteur method. Recently the third table has been used in a child, aged five years. The treatment was as easily borne as the less intensive. Since any wound, however slight, may

cause rabies, there seems to be no reason for difference in the manner of treatment. I incline to think that the intensive (third table) should be used in all cases.

FIRST FORMULA FOR TREATMENT EQUALS FIFTEEN DAYS.

Day of treatment.	Age of the dried cord.	Quantity of the emulsion.	Day of treatment.	Age of the dried cord.	Quantity of the emulsion.
1	14 days	3 c.c.	6	5 days	2 c.c.
	13 "	3 "	7	5 "	2 "
2	12 "	3 "	8	4 "	2 "
	11 "	3 "	9	3 "	1 "
3	10 "	3 "	10	5 "	2 "
	9 "	3 "	11	5 "	2 "
4	8 "	3 "	12	4 "	2 "
	7 "	3 "	13	4 "	2 "
5	6 "	2 "	14	3 "	2 "
	6 "	2 "	15	3 "	2 "

SECOND FORMULA FOR TREATMENT EQUALS EIGHTEEN DAYS.

Day of treatment.	Age of the cord.	Quantity injected.	Day of treatment.	Age of the cord.	Quantity injected.
1	14 days	3 c.c.	8	4 days	2 c.c.
	13 "	3 "	9	3 "	1 "
2	12 "	3 "	10	5 "	2 "
	11 "	3 "	11	5 "	2 "
3	10 "	3 "	12	4 "	2 "
	9 "	3 "	13	4 "	2 "
4	8 "	3 "	14	3 "	2 "
	7 "	3 "	15	3 "	2 "
5	6 "	2 "	16	5 "	2 "
	6 "	2 "	17	4 "	2 "
6	5 "	2 "	18	3 "	2 "
7	5 "	2 "			

THIRD FORMULA FOR TREATMENT EQUALS TWENTY-ONE DAYS.

Day of treatment.	Age of the dried cord.	Quantity of the emulsion.
First { morning..	14 days	3 cubic centimetres.
	13 "	3 " "
evening ..	12 "	3 " "
	11 "	3 " "
Second { morning..	10 "	3 " "
	9 "	3 " "
evening ..	8 "	3 " "
	7 "	3 " "
Third { morning....	6 "	2 " "
evening	6 "	2 " "
Fourth.....	5 "	2 " "
Fifth	5 "	2 " "
Sixth	4 "	2 " "
Seventh.....	3 "	1 " "
Eighth.....	4 "	2 " "
Ninth.....	3 "	1 " "
Tenth	5 "	2 " "
Eleventh.....	5 "	2 " "
Twelfth.....	4 "	2 " "
Thirteenth	4 "	2 " "
Fourteenth	3 "	2 " "
Fifteenth.....	3 "	2 " "
Sixteenth.....	5 "	2 " "
Seventeenth.....	4 "	2 " "
Eighteenth	3 "	2 " "
Nineteenth	5 "	2 " "
Twentieth.....	4 "	2 " "
Twenty-first.....	3 "	2 " "

An important addendum and adjuvant to the Pasteur treatment is that of Dr. Roux, sous-directeur de l'Institut Pasteur. The entire brain and medulla oblongata of the rabbit dead of a fixed virus is immersed in ether and remains in

it for 48 hours. It is then taken out and allowed to remain uncovered for one hour; afterward it is finely triturated in a mortar, adding gradually 40 c.c. of sterile water. This emulsion is permitted to stand and settle for one hour, though a much less time is sufficient. Of the supernatant fluid 10 c.c. are subcutaneously injected into the walls of the abdomen, in amounts of 5 c.c. injected on one and the other side of the abdomen. The hypochondria and flanks are less sensitive. This operation is repeated once on some subsequent occasion. It is desirable that these injections should be given as early as possible. This method has been used by the writer in every case, now 368 in number, the youngest 14 months, the oldest over 80 years; and in two patients pregnant six months; there were no bad results in any case; indeed, it seems to be better borne and less painful than the ordinary injections.[1]

Treatment is preventive, but it has no curative effect. Rabbits, chickens, mice, dogs, sometimes recover from the earliest symptoms, but do not survive the development of later signs. If a human being contract rabies he inevitably dies. Those bitten should resort to treatment at once;

[1] See p. 364.

delay may be deadly. A physician consulted me regarding a bite on his thumb. He had already delayed ten days and proposed further to await the result of an inoculation experiment. He was advised to take treatment at once, but failed to do so. He developed rabies about as soon as the inoculated animals. Two patients were advised to submit to treatment immediately. They refused, stating that they would await the result of the inoculation experiment. Rabies developed almost simultaneously in the experiment animals and the patients. A boy, aged eight years, was brought by his father for treatment. He received two hypodermic injections, 5 c.c. each of emulsion of brain and medulla oblongata. The child made little complaint, but the parent, much excited, vehemently declared that the treatment would kill his child. Against the most earnest protestations he took the child home next day, which was February 5th, 1900. The wounds were multiple and severe. One on the right side of the forehead, one over the right eyebrow, one on the posterior surface of the right upper arm, and one on the right scapula. These wounds had been cauterized with nitric acid and washed with solution of corrosive chloride of mercury

30 minutes after they had been received. Three rabbits subdurally inoculated from the medulla oblongata of this dog developed rabies on February 19th and 20th, 14 and 15 days after the operation. A cow bitten by the dog also died of rabies. On February 25th, 1900, the child returned for treatment after an interval of 20 days' suspension. Rabies developed in the child on March 14th, 40 days after he had been bitten and 16 days after resumption of treatment. The child died on March 17th, 1900. A girl, aged six years, was brought to this institution May 23d, 1901, with rabies already developed. She died in one and one-half hours after her arrival, and about 30 days after having been bitten. The wound was across the bridge of the nose on the left side, and had entirely healed. However, a number not treated escape. An example of this was a girl, aged ten years, bitten severely on both bare arms. The dog had been experimentally demonstrated rabid.

Cauterization reduces the liability to rabies almost one-half. It should be early resorted to, but in many cases it is not possible for it to follow the intricacies of the wounds. Immersing the wounded part several times daily in very hot

water, to which boric acid may be added, is useful. Serum therapy as a mode of treatment has not achieved success. The following is from Sternberg's "Bacteriology," pp. 334, 335: "In 1894 Tizzoni and Centanni gave an account of experiments made principally upon sheep. By repeated inoculations they succeeded in obtaining from these animals a serum having an immunizing value of 1:25,000 or more, and from this a precipitate was obtained estimated to have a value of 1:300,000, and which in doses of 0.23 gm. (of the dried precipitate), dissolved in five times its weight of water, ought to be a sufficient dose to protect a man from the development of hydrophobia. The authors believe that inoculation with this antitoxin would be reliable for man, and would possess decided advantages over Pasteur's method. These advantages are specified as follows: Applicability at any time during the period of incubation up to the moment of the appearance of the symptoms of rabies; absolute absence of virulence and of any injurious action; very rapid treatment by the injection of one or several small doses of material; complete solubility and consequently prompt absorption of the material injected, and its long

preservation in a dry condition." "He doth protest too much." Seven years have elapsed since these statements were made but no further information has been given. An efficient antitoxin remains an unsatisfied desideratum, and "a consummation devoutly to be wished."

D. P. Blaine, professor of animal medicine, London, about 1818, gives a cure for rabies: "Fresh leaves of the tree box, ℥ ij., of rue, ℥ ij., of sage, ℥ ss." His remark, as follows, is more sage than his remedy: "Out of ten dogs bitten, I believe not more than two on an average escape; but of the same number in the human subject bitten, perhaps not so many as two would become hydrophobious."

Intravenous Injection.—This mode of treatment has not been practised sufficiently often in the human being to determine its efficacy and freedom from risk.

Drs. Novi and Poppi communicated (April, 1892) to the Medico-Chirurgical Society of Bologna a case styled the first cure of a grave case of rabies by intravenous injections; which case has been received with incredulity since Drs. L. de Blasi and G. Russo-Travali failed to cure or to alleviate three cases of rabies treated in like

manner. 1st, a girl, aged six years; 2d, a boy, aged seven years; 3d, a man, aged 57 years. The boy and girl were undergoing treatment when rabies developed; thereupon the intravenous injections were given, which were of cords that had dried five, four, and three days. The dose was 3 c.c. of each. The man above referred to had been treated at the Institute of Palermo from December 19th, 1894, to January 9th, 1895, for a previous bite. On September 7th, 1895, he was again bitten by a rabid dog. The wound was on his right hand. He died of rabies December 10th, 1895, notwithstanding intravenous injection. His previously acquired immunity did not last one year. This constitutes an inexact reply to the question, How long does treatment confer immunity?

Dr. Rambaud, director of the New York Pasteur Institute, reports four cases undergoing treatment, to which intravenous injections were superadded. The cases were three in boys, aged four, nine, and ten years, respectively, and one in a girl, aged nine years. The nine-year-old boy and girl received each nine intravenous injections in doses of 2 c.c. and 3 c.c. The veins injected were cephalic, basilic, median cephalic,

and median basilic. These children had not developed rabies. The most virulent emulsion used was that of a fourth-day cord.

Some Peculiarities of Rabic Virus.—Sternberg asserts that "the virus fixi is destroyed by exposure for ten minutes to a temperature of 60° C. (140° F.), and that a temperature of 55° C. (131° F.) fails to destroy in ten minutes. Marie states that it can be destroyed by heating to 48° C. (118° + F.) for five minutes, a sojourn of one hour at 50° C. (122° F.), or of 24 hours at 45° C. (113° F.) suffices to cause the rabic bulb to lose all its virulence." It is very slowly destroyed at 108° F., and not rapidly, as was stated through error in Vol. XV, p. 521.

De Blasi and Russo-Travali filtered "sur bougie" emulsions of the rabic bulb and injected the filtrate into rabbits which succumbed to paralysis. Galtier submitted to a temperature of more than 100° C. (212° + F.) the nervous emulsions of rabid animals, and inoculated them into the veins and serous spaces of dogs, sheep, and goats. The animals presented the phenomena of grave intoxication, sometimes mortal. Of course, this was the effect of the toxin.

The latent period of rabies which precedes the symptomatic reaction of the malady seems to prove that the rabic virus acts on the nerve centres in secreting a poison—a toxin, of which a certain quantity and a prolonged action upon the cells are necessary for the development of the specific symptoms.

Rabbits inoculated subdurally with the rabic toxin either take nothing, or if they develop paralysis their medullas inoculated convey no rabies.

Sheltered from the air, cold — 24° C. (— 11° F.) and 4° C. (40° F.) has no effect whatever on the rabic virus. The brain of a rabid rabbit has shown itself active even at the end of five months (Viala). Jobert preserved the body of a rabbit for more than ten months at — 10° C. (14° F.) and — 25° C. (— 13° F.), and the bulb nevertheless remained virulent. Cold of — 35° C. and — 60° C. attenuated the virulence without destroying it.

The rabic virus preserves its strength for a rather long time in the cadaver, even in a state of putrefaction. Galtier has succeeded in the transmission of rabies by inoculation of the nerve centres from cadavers of rabbits buried

23 days and from dogs buried 44 days. A practical difficulty in determining the existence of rabies in dead animals is the rotten state in which they are received, for the putrefactive organisms kill the experimentally inoculated animals. Putrefactive material, in neutral glycerin, changed as often as its odor remains, has the rabic virus preserved and the putrefactive virus eliminated—destroyed. The glycerin must be neutral and not superabundant. If the glycerin becomes acid, as it is liable to do, the rabic virus is destroyed; and perhaps the same result takes place in vaccine virus. Neutral glycerin at 30° C. (86° F.), other conditions being equal, is without action on the rabic virus. The bulb of rabid rabbits, preserved for four weeks in glycerin at the temperature of the room, gave the disease as rapidly as the fresh virus. An emulsion rendered decidedly acid to reactive paper by one or two drops of acetic acid or decidedly alkaline with a small crystal of carbonate of soda shows itself inoffensive. Phenic acid destroys the rabic virus in one or two hours, according to its concentration of 5 per cent. or 2 per cent. Boric acid is active in 15 minutes; lemon juice in seven minutes. Nitrate of silver, so often employed, is

feeble in action. Sulphate of copper, aqua ammoniæ, hydrochloric and sulphuric acids are active. According to Bakai a solution of ten drops of chlorine in 10 gm. of distilled water destroys the virus completely; it is likewise so with bromine water and the essence of eucalyptus. A solution of 1:1,000 mercury bichloride, freshly made, renders virus inert. Solution of permanganate of potassium, 5 per cent. to 2 per cent. in alcohol at 50° to 90° after 24 hours, destroys the virus. The emulsion in alcohol, 25°, inoculated after 24 hours and after three days gave rabies after periods of inoculation which were respectively eight and ten days. Inoculated after five days it showed itself inactive. Alcohol at 15° did not alter the virulence after a contact of seven days. Simple water conserves the virulence from 20 to 40 days; so also do bouillon and 0.6-per-cent. salt solution.

The gastric juice exerts an attenuative action on the rabic virus after a sojourn of five hours at a temperature of 20° C. Tizzoni and Centanni utilized this property to obtain a vaccine for sheep, rabbits, and dogs, injecting in them an emulsion prepared after this method. Marie

says: "On the same order of ideas we desire to say a few words on the action of bile. Bile, either from a rabid or well rabbit, and emulsion of rabic bulb in equal parts is sterile. Franzius thought that this could be availed of as a protective. He regarded it as of the nature of an antitoxin. Valé, repeating his experiments, found that there was no antitoxic action, but that the bile acted as a powerful antiseptic."

In the East the raw livers of rabid dogs are given by the mouth to those bitten.

Light acts powerfully on rabic virus. An exposure of 40 hours to sunlight destroys the rabic virus even if the thermometer does not exceed 30°. The increase of atmospheric pressure has no influence whatever, nor have the Roentgen rays.

The immunity given to herbivora and in some cases to dogs by intravenous injection of rabic virus constitutes one of the most obscure questions in the history of rabies. The facts reported in 1881 by Galtier are exact. The injection of rabic saliva, or, better, an emulsion of rabic bulb into the jugular vein of sheep or horse, does not cause rabies and may confer immunity. MM. Roux and Nocard, in their work

on this subject, maintain that it is possible so to protect herbivora even after 24 hours following intraocular injection with street virus.

Protopopoff at the same time showed that the intravenous injection of the graduated virus in the dog did not kill it, but gave it immunity. Four dogs were inoculated in the femoral vein with cords of the sixth, third, and first days. After some time they were injected anew in their jugulars. In about a month they were tested by trephining and subdural injection with the bulb of fixed virus. They all remained well. M. Roux established that it was possible to render dogs refractory, injecting them only one time in the veins with a large quantity of cords of very feeble virulence, that of the eighth or eleventh day; but the result was not so constant as in herbivora. In order to explain the foregoing surprising facts Helman ascribed them to the structure of the vessels. The capillaries in the herbivora would oppose themselves to the passage of the virus into the nerve centres, while they would permit it in other animals. The history authorizes no such interpretation. The injection in sheep practised not in the jugulars but in the carotids may be followed by the develop-

ment of rabies. Inoculated, on the contrary, in the crural artery, the rabic emulsion leaves the animal well. If the rabic virus becomes inoffensive in passing extremely diluted through the pulmonary filter, we do not understand why it should not be so for other animals than the herbivora, and why the injection into the auricular vein should give rabies to rabbits.

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Bacteriology, by Dr. G. M. Sternberg.

Immunisation antirabique au moyen des injections intravasculaires par le docteur V. Krasmitski, Institut Bactériologique à Kiew, Annales de l'Institut Pasteur, June 25, 1902.

THE FALLACY AND INUTILITY OF THE SO-CALLED " RAPID DIAGNOSIS OF RABIES."

There are two methods, both expeditious, both untrustworthy; in both the diagnosis is defective in the abstract, and also as applied to the determination of the question " to be or not to be " treated. As regards the first, the morbid histology of the nerve ganglia (elaborated, not originated, by von Gehuchten and Nelis), it is untrustworthy, because its absence is no proof that rabies is absent; and if it is present, the same histology is also present in other diseases, markedly in tetanus, but likewise in many infectious diseases. Even conditions of decomposition, in which state the animal is most frequently received, produce like appearances; from this cause also sections of normal ganglia, in spots, often exhibit these changes.

" In my memoirs on the pathology of the spinal ganglia, I (Babes) have described similar lesions in many diseases "; he also notes that the number of cells bordering the elements

(nerve cells) " multiply themselves with facility as a result of different irritations." This last sentence indicates the essential morbid morphology, and refutes its specificity.

As regards the second, the Negri bodies, so named from their discoverer, are found especially in the hippocampus major and are alleged to be surely diagnostic of rabies, and to be found in no other disease; but their absence is not alleged to exclude rabies. These bodies are of two varieties, one taking an eosin stain, the other a methylene blue. The former are ovoidal, club-like, or crescentic, not unlike malarial crescents. Some are large, some are small; in some the entire surface is beset with minute round masses, somewhat projecting; some are opaque white, some translucent, a few are arranged in circlets; sometimes the body contains only a few larger ones or a single one larger still; they sometimes strongly resemble cell vacuoles, so misnamed. Most of these bodies stain vividly; but some, numerous and grouped together, stain of a dull brownish-red color, and their contour is irregular, as if shrunken; in shape they tend to oval or quadrilateral. There are also blue-staining bodies exactly like those described; in size both

are medium, between the large and small ones. Some blue cells are of large size, globular, with unstained protoplasm divided up into roundish corpuscles by a process which may be likened to segmentation. Sometimes they are traversed by irregular radial lines, like fissures.

It is not the object of this article to describe, with accurate detail, the morphology or technique of the Negri bodies; these may be found in Dr. A. Negri's essay in the Beitrag zum Studium der Aetiologie der Tollwuth in *Zeitschrift für Hygiene und Infectionskrankheiten,* xliii, 3.

It is contended that the bodies in question are protozoa, or, if not, that they are specific degenerations produced by rabies and by no other disease. This latter qualification may have had its suggestion in the fact that some in search of these organisms have erred from the truth and found only pseudoprotozoa. Why may not these bodies be the result of cloudy swelling and vacuolation, or changes of morphology taking place in decomposition, under conditions of inhibition, producing enlargement, distortion, and disfiguration of normal cell structure? These degenerations are common to many diseases and causes. The fore-

going are merely hypothetical suggestions. What these bodies (Negri) may be (see Addenda) is immaterial to the fact that I have frequently found them in rabbits dead of ordinary infection, often from wounds received in fighting, which become infected from the pens in which these animals are kept. These bodies were found in a dog accidentally killed, run over by an automobile, also in another dog which died of rupture of its stomach. Rabbits subdurally inoculated from the medulla oblongata of both these dogs failed to show rabies, although the experiments were repeated in each case, on each occasion using two rabbits. The preponderance of probability is in the direction of negation of the presence of rabies.[1]

The inhibitory condition above referred to, used in these experiments, is simply that of placing the dead body on ice for 24 hours, then removing the brain and keeping it on ice for 24 hours more, then keeping the excised hippocampus on ice for 24 hours.

As bearing upon treatment, these preliminary examinations fail to settle the question of " to be or not to be " treated. If the foregoing appearances are found, treatment would be ad-

[1] See Appendix II.

vised, notwithstanding that they may be present when rabies is absent. Since they may be absent when rabies is present, surely no one on this account would advise against treatment. In point of fact, persons bitten are going to be treated anyhow, and any delay is worse than useless.

The trend of events is about as follows: The circumstances in the case arouse suspicion of rabies, and those concerned desire to have such suspicion dispelled, in order that persons bitten may not be required to undergo treatment, or that lower animals may not become sources of danger and apprehension, making their destruction advisable. The usual phraseology is: "Doctor, we want to know whether this dog was mad or not." They really earnestly desire to know that the dog was not mad. The public erroneously think that this can and ought to be easily proved, not only "beyond a reasonable doubt," but with absolutely certain demonstration. These statements refer, of course, to the negative proposition, *i. e.*, the proving by animal inoculation that the animal under investigation was not mad, for the reason that the inoculated animals did not acquire rabies. Sometimes an

animal may not be susceptible, which is rare and can easily be corrected by using a number of animals; there may be an error of technique, which also can be avoided. The most common cause and source of most serious mistake resides in the fact that the rabietic virus has been present, but has been destroyed. A carcass lying in the intense heat and light of a summer sun may become inert; an exposure of rabietic virus to sunlight for 40 hours destroys it, though the temperature may be only 86° F. The virus is very sensitive to heat and easily attenuated, weakened, even when not destroyed. Decidedly opposite is the effect of cold: I have had a cat frozen stiff, and the virus remain unaffected. "Sheltered from the air, 11° F. has no effect." Jobert preserved the body of a rabbit at 14° F. "and at — 13° F., and the bulb, nevertheless, remained virulent." Temperatures of — 35° and — 60° C. attenuate, but do not destroy the virus. Decomposition does not necessarily destroy it; Galtier produced rabies from the nerve centres of a dog that had been buried 44 days. Placing the rotten material in neutral glycerin, and renewing it until the odor has disappeared, will eliminate the organisms of putrefaction and render the

specific virus fit for inoculation. The rabietic virus can be preserved in glycerin, but the glycerin must be neutral and remain so. A medulla oblongata of a rabid rabbit, immersed in glycerin in a glass-stoppered phial, was brought from the Institut Pasteur, Paris. From this medulla four rabbits were, subdurally, inoculated upon the brain without effect; they simply "waxed fat and kicked." Why? Because, in making the sea voyage, the glass stopper became loose and the glycerin acid. Acid or alkaline glycerin should not be used. Suppose the above mentioned medulla had been that of a dog that had bitten a number of persons severely on the head, face, and neck. If, as a result of this fallacious experiment, they had been assured that the dog was not mad, they might have been aroused from a false sense of security by the realization of a terrific calamity. Even though a dog or other animal should remain alive after a sickness, it is not absolutely certain that it was not rabies. An animal may die, and at the post-mortem examination sufficient cause for death may be found, and yet rabies may have coexisted. I have the heart of a dog which is packed full of the worm known as *Filaria immitis*. This dog

bit a policeman, who was treated without delay. Rabbits subdurally inoculated from this dog had rabies; the policeman did not.

Negative evidence must be sceptically considered and very carefully weighed; proving a negative is often a " doubtful balance of rights and wrongs "; at its best it is a preponderance of probabilities. The only absolute certainty is the demonstrated affirmative proof afforded when inoculated animals have rabies, and another series inoculated from these also have rabies.

In institutions prophylactically treating hydrophobia (Pasteur method), two rabbits are inoculated daily, in series, which the Institut Pasteur, Paris, has been doing for about 21 years. During this period rabies has been given serially to about 15,330 rabbits; the Pasteur Institute, of Baltimore, has been doing the same for more than nine years, giving rabies serially to about 6,570 rabbits. Thus this disease has been propagated serially in about 21,900 rabbits. The data from all the antirabietic institutions are not available, but it is safe to assert that they would enormously increase the numbers given. That the disease of the nervous system termed hydrophobia (rabies) is produced by the contagion

of a specific virus is supererogatively overproved by these figures.

The human animal never recovers from an attack of hydrophobia (rabies); this the lower animals sometimes, but seldom, do. Cases are recorded in which it is alleged that persons have recovered, but these cases do not bear critical scrutiny, and have not received scientific acceptance.

The treatment is by hypodermic injection, and does no harm under any circumstances, but almost without exception the general health improves.

CONCLUSIONS.

1. The presence of the ganglionic changes, described by von Gehuchten and Nelis, or the presence of the structure termed Negri bodies, is not pathognomonic of rabies (hydrophobia), since these are often found when rabies does not exist.

2. The absence of one or both of these appearances does not prove that rabies is absent, since they may be present when rabies is absent, and absent when rabies is present; therefore they are not infallible indications of rabies (hydrophobia).

3. In the exigency of treatment, the results of preliminary examinations should not be waited for. When the circumstances are suspicious, when the animal has been killed or has escaped, when a person has reason to think that he has been in contact with the virus of rabies (hydrophobia), he should, as soon as he can, consult his physician, and, preferably through him, should at once communicate with some reputable institution treating this disease preventively, and abide by the advice given.

ADDENDA.

The experiments made by the writer were done throughout the month of June, 1906.[1] On November 14th, 1906, the October number of the *Annales de l'Institut Pasteur* was received. On page 859 is an article by Y. Manouélian (Travail du laboratoire de M. Metchnikoff). The title is " Recherches sur le mécanisme de la destruction des cellules nerveuses." The writer asserts that the destruction and disappearance of the nerve cells (cerebrospinal ganglia) in rabies are effected by phagocytosis, and that the macrophages, described by M. Metchnikoff, are the

[1] Published in the *New York Medical Journal,* February 23, 1907.

agents in breaking up and removing the nerve structure which has become useless or harmful, so rendered in this instance by the virus of rabies. These macrophages, figured in Plate XXXII by M. Manouélian, morphologically are identical with those figured by Dr. Negri, and designated as protozoa, causative of rabies (Figs. 1, 4; except 6, "parasitäre Gebilde"). M. Manouélian in his article nowhere mentions Dr. Negri or his work. So far as appears, the work of the former was done without any knowledge of the work of the latter. Both these investigators were working with rabietic material. The writer of this present article was working with non-rabietic material; yet all these investigations reveal the same morphology. Evidently these forms have no causal relation to rabies, and M. Manouélian does not so allege; on the contrary, he notes that these bodies, these cells, are the large phagocytes, macrophages, described by M. Metchnikoff as active in removing the worn-out nerve tissue of the aged; the tissue which the unknown virus of rabies has vitiated these known cells remove. The bodies of Dr. Negri, mistaken for specific protozoa, are the macrophages of M. Metchnikoff, which are common carriers, and in no other sense specific morbific agents.

REPORT OF THE FIRST THOUSAND CASES TREATED AT THE PASTEUR INSTITUTE, BALTIMORE, MD.

It is worthy of note that 632 of the 1,000 persons treated were bitten by animals absolutely proven rabid; see columns A and B.

A—Animals demonstrated rabid by cerebral, subdural inoculation of rabbits.

B—Other animals or human beings developed rabies as a result of the bite.

C—Symptoms those of rabies, but not demonstrated.

D—Escaped observation; no reliable history.

E—Wounds not the result of bites.

F—Inoculation of rabbits, as in A, without result.

Of the 1,000 persons treated 719 were males, 281 were females; 323 were children up to and under ten years of age, being 32 per cent. of all patients treated.

From 10 years of age to 20 years, 201 patients.

From 20 years of age to 30 years, 167 patients.

		A			B			C			D			E			F		
Bites inflicted on head, face and bare neck	Single		38	97		2	9		6	20		8	22		4	5		1	6
	Multiple		22			4			9			9			0			2	
	Severe and multiple		37			3			5			5			1			3	
Cauterization	Efficient	10			0			3			5			0		0		
	Non-efficient	54			6			10			8			4		5		
	No cauterization	33			3			7			9			1		1		
Bites inflicted on hands	Single		95	249		12	35		40	91		24	66		16	26		10	18
	Multiple		106			15			33			24			9			6	
	Severe and multiple		48			8			18			18			1			2	
Cauterization	Efficient	44			8			23			10			5		2		
	Non-efficient	109			19			28			19			11		6		
	No cauterization	96			8			40			37			10		10		
Hands	Covered	12			3			10			1			0		0		
	Uncovered	237			32			77			64			24		16		
Bites inflicted on limbs	Single		73	199		14	28		33	80		21	52		2	3		7	14
	Multiple		73			11			36			26			0			4	
	Severe and multiple		53			3			11			5			1			3	
Extremities	Upper	70			14			34			18			2		5		
	Lower	121			11			47			34			1		9		
Cauterization	Efficient	34			4			15			9			1		1		
	Non-efficient	112			10			42			24			1		8		
	No cauterization	53			14			23			19			1		5		
Clothes torn		138			11			65			35			2		12		
Bites inflicted on body	Single		5	13		0	2		0	2		5	11		0	0		0	2
	Multiple		4			1			0			6			0			2	
	Severe and multiple		4			1			2			0			0			0	
Cauterization	Efficient	2			1			0			3			0		0		
	Non-efficient	8			1			2			4			0		2		
	No cauterization	3			0			0			4			0		0		
Clothes torn		13			2			2			7			0		1		
				558			74			193			151			34			40

From 30 years of age to 40 years, 148 patients.

From 40 years of age to 50 years, 67 patients.

From 50 years of age to 60 years, 54 patients.

From 60 years of age to 82 years, 35 patients.

Age unknown, five patients.

The youngest treated was seven months old, the oldest 82 years.

These 1,000 persons treated came from:

Alabama	2
Arkansas	8
Delaware	38
Georgia	12
Indiana	2
Louisiana	36
Maryland	334
Massachusetts	1
Mexico	1
Mississippi	3
New Jersey	5
North Carolina	117
Ohio	11
Pennsylvania	102
South Carolina	51
Tennessee	4
Virginia	104
Washington and District of Columbia	57
West Virginia	112

Eighty-five per cent. of the patients were from rural districts.

The wounds were inflicted by dogs in 874 cases, in 65 cases by cats, in one by a calf, in one by a pet pig, in seven by cows, in nine by horses, and in four by human beings. In 39 cases the wounds were not the result of bites.

Seven hundred and forty-six persons came to receive treatment during the first week after having been bitten, 146 the second week, 36 the third week, 22 the fourth week, 26 the fifth week, 11 the sixth week, two the seventh week, and two the eighth week, and five the tenth week. In four cases the date is uncertain.

In 40 cases the treatment was discontinued, because the animal held under observation was evidently not rabid.

Five patients enceinte were treated without untoward result.

Of the 1,000 persons that completed the period requisite for immunity two are reported to have died of hydrophobia. One had chronic Bright's disease before and during treatment. The differentiation of similar symptoms is not scientifically exact. If accepted, the rate of mortality is only one-fifth of 1 per cent., much less than the usual rate, which is one-third of 1 per cent.

June 1, 1907.

Supplementary Note, February 1, 1909.

To this date there have been admitted for treatment 1,300 cases. There has been one additional death, making the total number of deaths to this date two, mortality .153 per cent. Of these 300 additional patients, 126 belong in column A and 10 belong to column B, making a total of 768 demonstrated rabid animals. These 1,300 patients were treated in the period from February 21st, 1898, to February 1st, 1909, inclusive. On pages 336-337 we append a table of all cases of rabies observed at the Pasteur Institute, Baltimore.

Following is a table of all animals examined at Pasteur Institute, Baltimore, for rabies, with results:

Animals.	Positive.		Negative.
Dogs	438		112
Cats	30		19
Horses	6		4
Cows	10		3
Calves	2		—
Sheep	1		—
Pigs	2		—
Mule	—		1
Human	6		—
Squirrel	—		1
Total	495	+	140 = 635

CASES OF HYDROPHOBIA (RABIES) OBSERVED AT

Cases of rabies (human).	Sex.	Age.	Occupation.	Date of bite.	Seat of bite.
I.—R. N.	M.	8	School-boy.	February 2, 1900	Right arm and scapula; right side of forehead over right eyebrow.
II.—L. C.	F.	6	School-girl.	May 23, 1901	Across bridge of nose.
III.—J. J. P.	M.	59	Farmer.	March 1, 1902	Right hand and right thigh.
IV.— ?	F.	65	.... ?	..... ?	..... ? .....
V.—H. A.	M.	18	Laborer.	November 19, 1902	Right hand — dorsal and palmar aspect.
VI.— ?	M.	9	.... ?	..... ?	..... ? .....
VII.—Y. D.	M.	8	School-boy.	February 17, 1904	Three on left side of face and four on left thigh.
VIII.—S. A. B.	M.	45	Farmer.	December 6, 1903	Right forearm.
IX.—H. C. H.	M.	25	Foreman.	November 8, 1904	Right cheek and angle of mouth; left wrist.
X.—C. W.	M.	3	None.	September 8, 1905	Bridge of nose; through nasal septum and lips.
XI.—J. S.	M.	9	School-boy.	February 11, 1908	Cheek torn through in two places; left eyelid torn through.
XII.—F. R.	M.	10	School-boy.	February 11, 1908	Upper lip.
XIII.—W.	F.	6	None.	May 23, 1908	Through upper lip into nares and through nasal septum, crushing it; left commissure of mouth and under the chin.
XIV.—L. M.	M.	11	School-boy.	About July 1, 1908	Scratch on right cheek.
XV.—W. T.	M.	52	Laborer.	About July 3, 1908	On finger.
XVI.—E. T.	M.	30	Laborer.	About Sept. 23, 1908	On face.

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racter of tes.	Cauterization.	Date of development of rabies.	Incubation period.	Remarks.
ere.	Efficient.	Mch. 17, 1900	40 days.	Patient taken away after first treatment on February 4, 1900, and did not return until February 25, 1900; patient developed and died of rabies during treatment.
ere.	None.	June 20, 1901	28 days.	No treatment; had rabies when she came to the hospital.
ere.	Efficient, but late.	April 5, 1902	35 days.	Developed rabies 10 days after end of treatment.
....	..... ?	... . ?	106 days.	Cat bite; not treated; case seen outside the hospital.
ere.	Non-efficient.	Dec. 13, 1902	24 days.	Not treated; had disease on admission to hospital; frequent seminal emissions; maniacal and bit 1st medical assistant.
....	..... ?	..... ?	..... ?	Not treated; had rabies when admitted to hospital.
ere.	Efficient.	Mch. 21, 1904	32 days.	Developed rabies six days after end of treatment.
ht.	Efficient, but late.	.....	.....	Reported to have died of rabies. In reality, he died of uremic coma of Bright's disease.
ere.	Efficient, but late.	Dec. 12, 1904	34 days.	Developed rabies two days before end of treatment.
re.	Non-efficient.	Nov. 14, 1905	67 days.	Developed rabies 35 days after end of treatment; treated 32 days.
re.	Efficient.	Mch. 12, 1908	30 days.	Developed rabies seven days after end of treatment.
ht.	Non-efficient.	Mch. 12, 1908	30 days.	Developed rabies five days after end of treatment.
re.	Non-efficient.	July 14, 1908	52 days.	Under treatment at time of development; treated 53 days and died 54 days after bite; rabies developed 32 days after end of usual 21 days' treatment.
ht.	None.	Aug. 1, 1908	About 30 days.	Not treated; had rabies on admission to the hospital.
ht.	None.	Oct. 8, 1908	About 97 days.	Not treated; had rabies on admission to the hospital.
ht.	None.	Nov. 5, 1908	About 43 days.	Not treated; had rabies on admission to the hospital.

THE PERIOD OF INCUBATION.

Early Development.—Persons bitten or otherwise in contact with rabies virus very reasonably ask how soon may the disease come on and how late. This question may be answered by relating the following cases:

CASE 1.—Gustave Coudurier, age 7 years, bitten June 9th, developed rabies June 24th: incubation, *15 days.*

Situation of Bites.—One wound on the head about 3 inches long, right upper eyelid torn through. Two inoculated guinea-pigs developed rabies. (Annales de l'Institut Pasteur, Vol. III, 1889, p. 399.)

CASE 2.—Louis Allegre, age 14 years, bitten December 25th, 1888; developed rabies January 10th, 1889, and died January 14th, 1889: incubation, *16 days.*

Situation of Bites.—Nine bites on fingers and back of left hand, three are deep. The right hand had two bites, one on thumb and one on index finger, very penetrating. These wounds were very bloody; they were cauterized by a doctor five hours after the bite with thermo-cautery, but wholly without effect because of the number and depth of the wounds. (Annales de l'Institut Pasteur, Vol. III, 1889, p. 47.)

The rabic virus in the above cases must have gone at once to the cerebro-spinal system; it requires 12, 15, 16 days to develop rabies when subdurally inoculated.

CASE 3.—Late development: Lindley Herbert, age 17 years, bitten on *August 1st, 1887,* by a stray dog, was treated at the Institut Pasteur from the 6th to the 18th of August. The bites were five in number and situated upon the left hand. They were all very penetrating, and had been cauterized by silver nitrate about an hour after the bite.

The first symptoms of rabies manifested themselves on *August 31st, 1892,* with pain in the left shoulder and in the region of the neck. *Death supervened on September 4th, 1892.* That is to say, five years and one month after the bite. (Annales de l'Institut Pasteur, Vol. VII, 1893, p. 223.)

Case 4.—Isaac Juda, 28 years, physician, bitten on May 25th, 1889, on the left finger of the right hand. The wound bled and was cauterized by Dr. Juda himself some moments after the bite by thermo-cautery. He was treated from the 3d to the 17th of June, and on the 8th of July, 1891, he had pains in the bitten fingers extending along the radial nerve. On the 9th he had *marked hydrophobia,* and died on July 11th, 1891. Incubation two years and two months. Observation of Drs. Sciaky and Misrachi. The above is probably *not* rabies. (Annales de l'Institut Pasteur, Vol. V, 1891, p. 623.)

The above cases in the absence of affirmative inoculation from the medulla oblongata will not receive scientific credence.

Case 5.—Albert Jennehomme, 30 years, bitten on July 15th, 1901, on his two hands—many bites—two very deep and bloody. Dog reported mad by veterinarian. Treated at the Institut Pasteur from July 16th to August 2d, 1901. On April 24th, 1902, he presented the symptoms of rabies and died the same day. Two rabbits were inoculated from his medulla oblongata without result. Incubation, *783 days.* (Annales de l'Institut Pasteur, Vol. XVI, 1902, p. 455.)

Case 6.—Ernest Lacombe, 30 years, bitten March 17th, 1891; six bites, both sides of left wrist and on left leg near the crest of the tibia. All the wounds are deep and bled. They were cauterized by thermo-cautery about 15 minutes after bite. He was treated from March 25th to April 14th, 1891. About December 10th, 1891, he was seized with yawning, which could not be controlled, and on December 20th, 1891, he experienced tingling in the left arm, and then violent pains in the wrist, extending to left forearm, arm and shoulder. On December 23d, 1891, he refuses to drink and exhibits aërophobia. On December 25th, 1891, he was seized with

delirium, becoming furious, and died. Incubation, *267 days.* (Annales de l'Institut Pasteur, Vol. VI, 1892, p. 143.)

CASE 7.—Lord Doneraile, 67 years, bitten January 13th, 1887, on the right hand. The bites were bloody and there are numerous small bites on the fingers of the right hand. One bite on the right thumb and one on the middle finger; these bites are bloody. Many small bites upon the fingers of the left hand. One bite upon the left thumb and three bites on the left index finger. They were deep and bloody. The hands were covered with skin gloves, which were torn. The hands were simply bathed with hot water. He was bitten by a tame fox. He was treated from January 24th, 1887, to February 21st, 1887, and was seized with rabies on August 24th, 1887. Incubation, *223 days.* (Annales de l'Institut Pasteur, Vol. I, 1887, p. 462.)

Dr. A. Yersin, in reviewing Bauer's "Incubation of Hydrophobia in the Human" (Münch. Med. Wochenschr., Nos. 37 to 39, 1886), gives the following table of incubative periods:

	Per cent. of cases.
1 to 19 days in	8.24
23[1] " 39 " "	28.43
40 " 59 " "	21.18
69[2] " 79 " "	15.30
80 " 99 " "	9.22
100 " 149 " "	7.65
150 " 199 " "	5.69
200 " 249 " "	.98
250 " 339 " "	2.35
1 year to 15 months in	1.18

[1](20?) [2](60?)

One-half of the deaths occur between the twentieth and sixtieth days. (Annales de l'Institut Pasteur, Vol. I, 1887, p. 254.)

This is, however, only an hypothesis. Conjectural hypotheses studied out in the study must be proven by demonstrated certainties worked out in the laboratory.

"If the animals do not exhibit rabies before a week or 10 days after having inflicted the bite, it may be taken for granted that there have been no infections in the cases, even although the canine-rabies, when developed, should prove to be of the most infective and deadly character, and although the wounds inflicted should be of the most extensive and dangerous kind. There is no evidence whatever to prove that a dog or any other animal merely in the incubation period of the disease (not at least until the final stages of incubation) is capable of imparting rabies with its bite; there being good ground to show that the salivary secretion is not in any or to the slightest extent charged with the 'virus or rabies germ' during any such stage of the malady." (From "Rabies, Its Place Amongst Germ Diseases, and Its Origin in the Animal Kingdom," by David Sime, M. D., London, 1903.)

The saliva of a rabid dog is virulent three days, some assert eight days, before he shows any marked symptoms; the period of observation should be fourteen days; a week is entirely too close to the danger-line.

Note.

Since the above was written the following case of rabies developing in thirteen days was

published in *Annales de l'Institut Pasteur,* June, 1909:

Durand René, aged two years, bitten November 11, 1908; there were three severe bites on his face. No cauterization. Treatment begun November 14; was seized with rabies November 24, and died November 28, 1908. The medulla oblongata of this child gave rabies to inoculated animals on the eighteenth day. The medulla oblongata of the dog that bit Durand gave guinea-pigs rabies on the twentieth day after inoculation.

THE RESULTS OF THE PREVENTATIVE TREATMENT OF RABIES.

In disease the desiderata are: abolition, prevention, cure. England (limited in extent and insular in situation), by muzzling all dogs within and quarantining all from without, has abolished hydrophobia. Muzzling has been discontinued, but quarantine of necessity must remain in force. In most countries, circumstances make this result unattainable. The question then becomes one of prevention, which is not absolute but partial.

It is true that the lower animals sometimes, but seldom, recover from the earliest manifestations of rabies, but no human being has ever recovered. Some cases have been reported as cured,[1] but they lack authentic scrutiny, and have not received scientific acceptation.

In order to show the effect of Pasteur's method of treatment I direct attention to the following comparison: "Out of 1,362 human beings that had been bitten by rabid dogs or dogs suspected of being rabid, there occurred

[1] Vol. IX, yr. 1895, Annales de l'Institut Pasteur. See Appendix I.

105 fatal cases. If the wound is properly cauterized the number of human beings attacked with hydrophobia amounts to 33 per cent. of the whole number bitten; where, on the other hand, if cauterization is not resorted to it amounts to 83 per cent."[2]

The effect of immunizing treatment can be seen in the preceding article and still better in the following tables which I have gathered from the reports of the Institut Pasteur, Paris: Taking all cases from 1886 to 1908, inclusive, we find that out of a total of 31,330 cases there were in all 238 deaths = .759%. Out of a total of 31,330 cases there were during treatment 50 deaths = .159%. Of the remainder 31,280 cases there were, within 15 days after finishing treatment, 61 deaths = .195%. Of the remainder, 31,219 cases, there were, after 15 days after finishing treatment, 127 deaths = .406%. Of the total, therefore, of 31,280 cases there were after treatment 188 deaths = .601%.

It is claimed that, analogous to small-pox vaccination, 15 days must elapse after the end of the treatment before its full effect can be ob-

[2] Von Ziemssen Cyclopedia, Vol. III, p. 476.

tained. Those developing hydrophobia within this period are not counted in the statistics of any anti-rabic institute as failures of treatment, because the treatment has not had time to produce its full effect, which is scientifically true. But that the treatment did fail to save those dying of this disease within this period of 15 days is also practically true. What the treatment can and cannot do is of vital public concern. Therefore, all the deaths, among those treated, at whatever time occurring after treatment, must be counted. The above tables, therefore, afford an answer to the question, how many of those treated take the disease? When all the deaths are considered the mortality is only four-fifths of 1 per cent.; this is also the rate when the biting animal has been experimentally proved as rabid.

Inoculations on the surface of the brain produce the disease in about 15 days. If, therefore, rabies manifests itself in man within this period the virus must have been conveyed to the nervous system at the time of biting.

The mortality may further be classified as follows: In 4,516 cases bitten by animals in which rabies was demonstrated there were 34 deaths = .752%. In 18,686 cases bitten by

animals in which veterinarians' certificates of rabies were had there were 71 deaths = .379%. In 8,078 cases bitten by animals in which rabies was suspected but not proven there were 22 deaths = .272%.

According to parts bitten the classification is as follows: In 2,753 cases where head was bitten there were 28 deaths = 1.00%. In 17,656 cases where hands were bitten there were 69 deaths = .39%. In 10,871 cases where members were bitten there were 30 deaths = .275%. In 31,280 cases there were 127 deaths = .406%.

The statistics of mortality at the Pasteur Institute of Paris,[4] arranged according to the years, are as follows:

Year.	No. Patients.	Deaths.	Mortality.
1886.....	2,671	25	.94
1887.....	1,770	14	.79
1888.....	1,622	9	.55
1889.....	1,830	7	.38
1890.....	1,540	5	.32
1891.....	1,559	4	.25
1892.....	1,790	4	.22
1893.....	1,648	6	.36
1894.....	1,387	7	.50
1895.....	1,520	5	.33
1896.....	1,308	4	.30
1897.....	1,521	6	.39
1898.....	1,465	3	.20
1899.....	1,614	4	.25
1900.....	1,420	4	.28
1901.....	1,321	5	.38
1902.....	1,105	2	.18

[4] Bibliothèque de Thérapeutique, Gilbert et Carnot, p. 114.

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Year.	No. Patients.	Deaths.	Mortality.
1903.....	628	2	.32
1904.....	755	3	.39
1905.....	727	3	.41
1906.....	772	1	.13
1907.....	786	3	.38
22 years.....	30,759	126	.41.—

The above are the entire statistics of the Institut Pasteur of Paris. They are very favorable, however considered.

The statistical reports from various institutions:

Institute.	Epoch.	No. Cases.	Deaths.	Mortality.
Budapest	1890 to 1905	32,508	129	.46
Paris	1886 " 1907	30,759	126	.41
Kharkoff	1892 " 1901	9,740	56	.59
Lisbon	1893 " 1905	8,844	44	.50
Algiers	1894 " 1905	5,395	19	.35
Lyons	1900 " 1906	5,374	6	.11
Naples	1886 " 1903	4,578	31	.60
Constantinople	1900 " 1905	4,100	15	.36
Marseilles	1893 " 1903	3,563	13	.36
Bucharest[5].....	1903 " 1905	3,091	0	.00
Jassy	1891 " 1905	3,038	5	.16
Milan	1889 " 1903	2,942	24	.83
Tunis	—— " 1906	2,490	9	.36
Rome	1889 " 1902	1,940	7	.37
Vienna	1894 " 1903	1,937	13	.68
Lille	1895 " 1902	1,807	4	.22
New York	1890 " 1901	1,608	10	.62
Berlin	1898 " 1902	1,416	6	.42
Florence	1889 " 1901	1,254	2	.15
Kasauli	1905 " 1906	1,145	7	.61
Sophia	1902 " 1904	1,081	6	.55
Varsovie	1900 " 1902	923	9	.97
Faenza	1898 " 1902	779	1	.12
Perm	1901 " 1902	600	5	.83

[5] I would call attention to the fact that they had during 1888, 1889, 1890 447 cases with five deaths, mortality 1.10 per cent. (See Prof. Dr. A. Högyes, p. 174.)

Institute.	Epoch.	No. Cases.	Deaths.	Mortality.
St. Petersburg.....	1901 to ——	592	1	.16
Pernambuco	1889 " 1903	486	1	.20
Le Caire	1899 " 1901	375	1	.26
27 Institutes		132,365	550	.415

The mortality tables of the Pasteur Institute of Baltimore, from February 21, 1898, to February 1, 1909, are as follows:

Total number of patients treated.....	1,300
Total number of deaths.....	8 = .6153%
Number of deaths during treatment.....	2 = .1538%
Number of deaths within 15 days.....	4 = .3081%
Number of deaths after 15 days after end of treatment	6 = .4621%

Statistical tables of the Institut Pasteur, Paris, and others have not set forth exactly the nature of the wounds. Slight, single and severe wounds have been massed together under the caption of wounds of the head.

Scientific requirements necessitate such classifications of wounds as follows:

I. CLASS. Bites. *a.* Through clothing.
b. On bare parts.
Wounds other than bites; virus applied otherwise than by bites.

II. ORDER. Head, face and neck.
Hands, feet and limbs (upper and lower).
Body.

III. GENUS. Slight. *a.* Single.
b. Multiple.
Severe. *a.* Single.
b. Multiple.

IV. SPECIES. Dog, cat, pig, horse, cow, man, etc.

V. VARIETY. Peculiarities of wound.

MORTALITY ACCORDING TO THE SEVERITY OF WOUNDS.*

Institute.	Year.	Head and face bites.			Hand wounds.			Foot and body wounds (through clothing).			Total.		
		Patients.	Deaths.	Mortality.	Patients.	Deaths.	Mortality.	Patients.	Deaths.	Mortality.	Patients.	Deaths.	Mortality.
Paris	1886–1895	1,503	19	1·26	9,551	48	·50	6,283	16	·25	17,337	83	·47
Turin	1886–1894	169	6	3·54	1,260	14	1·11	778	1	·12	2,207	21	·95
Naples	1886–1895	84	4	4·76	672	7	1·04	513	1	·19	1,269	12	·94
Budapest . . .	1890–1895	479	24	5·01	1,983	22	1·10	2,452	13	·53	4,914	59	1·20
a. Treatment by dry cord.		320	21	6·56	1,408	17	1·20	1,682	13	·77	3,410	51	1·49
b. Treatment by use of dilutions of the fresh, virulent medulla oblongata.		159	3	1·88	575	5	·86	770	0	·00	1,504	8	·53
Totals		2,235	53	2·37	13,466	91	·66	10,026	31	·30	25,727	175	·68

* Lyssa, by A. Högyes, Budapest, p. 177.

Unless such exact classifications are made statistics are inexact in detail, and deductions therefore inaccurate, *e. g.*, multiple and severe bites on head, face and neck give a greater mortality than a single slight bite in some other regions.

At present science can prevent the development of hydrophobia, but cannot cure it after it has developed; all cases cannot be prevented, but a greater percentage of those exposed to hydrophobia are prevented by the Pasteur method than of those exposed to small-pox by the Jenner method.

PRACTICAL NOTES ON THE TREATMENT OF THOSE BITTEN BY SUPPOSEDLY RABID ANIMALS.

Efficient cauterization reduces the liability to this malady 50 per cent.; the Pasteur method fails only in one-third of 1 per cent.; conjoined, they give the best results. Cauterization, when solely relied upon, is overestimated; when restricted to a very early time limitation it is underestimated. The earlier it is done the better, but it is never too late, if the wound is unhealed; or if a point of induration is present, which latter should be incised and then cauterized. Excision or incision of extensive cicatrices and the amputation of lacerated parts are impractical as a rule; a finger so lacerated as to be useless is perhaps better off than on. Extensive and intricate wounds should be intermittently cauterized. Cannot something be done to lessen the pain is a question often asked regarding cauterization. A little girl of five years, subjected to this minor operation, shrieked and protested vehemently; on its completion, which occupied 20 minutes,

she remarked: "Well, it didn't hurt so very much." For this reason general or local anæsthesia is usually uncalled for. These remarks apply to the caustics and the method about to be described. First of all we desire to protest against the so commonly used nitrate of silver. It is painful and inefficient; its penetrative action is soon checked by the formation of an insoluble albuminate; it leaves a dark, adherent scab, the removal of which in order to efficiently cauterize is painful, as also is the natural separation of the superficial slough.

The following list is interesting, though the numbers are too few to warrant definite conclusions. It is taken from Högyes' work, p. 180. In the vast majority of cases circumstances make it impossible to obtain efficient cauterization within 15 minutes. It will be noted that silver nitrate, which is a most inefficient caustic, heads the list:

	Number cauterized within 15 minutes.	Deaths.	Number cauterized after 15 minutes.	Deaths.
Silver Nitrate	30	2	722	9
Actual Cautery	7	1	60	0
Corrosive Subl.	4	0	45	1
Carbol. Acid	28	0	475	11
Caustic Potash	2	0	45	2
Acetic Acid	3	0	12	0
Creolin	1	0	1	0

	Number cauterized within 15 minutes.	Deaths.	Number cauterized after 15 minutes.	Deaths.
Iodoform	—	—	9	1
Nitric Acid	—	—	22	0
Pot. Permanganate	—	—	1	0
Hydrochl. Acid	—	—	15	0
Ammon. Chloride	—	—	2	0
Canthar. Plaster	—	—	27	0
Excision	—	—	4	0
Copper Sulph.	—	—	3	0
Alcohol	—	—	2	0
Chlorine Water	—	—	1	0
Sesqui-Chloride of Iron.	—	—	1	0
Chromic Acid	—	—	1	0

Out of 1,362 human beings bitten by rabid dogs or dogs suspected of being rabid, there occurred 105 fatal cases. If the wound is properly cauterized the number of human beings attacked with hydrophobia amounts to 33 per cent. of the whole number. When, on the other hand, if cauterization is not resorted to it amounts to 83 per cent.[1]

The physician should at once be sent for; pending his arrival the parts should be immersed in water as hot as can be borne; hot, saturated boric solution may be recommended for household use which cannot be safely done with bichloride of mercury. The physician should first apply to or immerse the part in a 1:1,000 hot bichloride solution. Care must be exercised in

[1] Bollinger, Von Ziemssen, Vol. III, p. 476.

the prolonged application of such solutions to the heads of infants. If the cicatrix is newly formed it may be opened up. The excision of the cicatrix may require consideration, but it has not been practised at this institute. Intricate wounds, as in the interior of the nose, may require the electro-cautery; even then the intricacies of the bite cannot always be reached. Such cauterization may require general anæsthesia under ether; this was thoroughly done at this institute in one case, but the child died of hydrophobia, though the treatment was continued until the supervention of the disease;[1] the wounds of nose, face, and head had entirely healed. If near the eyes close the lids and have assistants hold them shut and cover with gauze; so also with the nostrils. Inside the mouth the teeth and parts adjacent to the bites must be shut off with gauze. Have a sufficient number of assistants to control patient. Timid sympathy must not restrain a doctor's hands. A physician stated in print that he abstained from treating a child bitten by a mad dog because the child was too nervous; his experience probably did not include observation of the nervousness of a child with hydrophobia.

[1] For fifty-two days.

Cauterize as soon after the bite as you can, but cauterize whenever you can. It has been asserted that sometime after a bite has been inflicted it is too late to cauterize the site of the wound. The induration and the cicatrix may be the depot from which virus is sent from time to time into the system. How long may the virus remain in the place of deposit? It has been demonstrated (by the inoculation of rabbits) to have been present in the cicatrices of a male child of six years, dead of rabies, 34 days after having been bitten and two days after death, in all 36 days.[1]

That the virus remains and is latent in the wound is also indicated by the pains in the wounds which often exist at the onset of the disease, and the occasional supervention of inflammation at the site of the wounds.

"If it were done, when 'tis done, then 'twere well
It were done quickly;"

but

"Better late than never."

The opinion that any physician is competent to cauterize is erroneous. This operation requires skill and judgment.

[1] See Annales de l'Institut Pasteur, Vol. XVII, p. 293.

To continue, the method usually used by us is as follows: As a rule all wounds are cauterized when they can be detected in patients treated in this institute.

After having applied the bichloride or boric acid solution to the part bitten, or having soaked it in the same, dry the part; apply with cotton wool mop so shaped as to fit the crevices of the wounds, strong carbolic acid solution; immediately take another mop and apply nitric acid, whereupon a slight explosive puff takes place; after this neutralize the nitric acid with saturated solution of bicarbonate of soda, and wash off with alcohol, which arrests the action of the carbolic acid. Dress the wounds dry, retaining the compress in place by bandage or adhesive plaster; in some cases collodion application may be used. If the slough or scab is sterile, as is often the case, further applications to the wound should be avoided. The compress and bandages may be removed when cleanliness necessitates. Pain is an evil and the surgeon should relieve it and avoid causing it because he is in a hurry, and because it is more convenient to jerk off a compress than to soak it off; to do so is a violation of that law which forbids the infliction of unnecessary pain on any creature.

The wounds should be allowed to heal under aseptic scab unless complications, *i. e.*, infection, suppuration, etc., prevent.

Determination as to Whether Biting Animal is Rabid and Whether Patient is to be Treated.

I. What should be done with the canine? If the dog can be kept so that he cannot escape and cannot do harm, he should be kept under observation for 14 days, preferably in his usual surroundings, if they are good; if this cannot be done he should be put in charge of a veterinarian or some association caring for animals; from both (the latter being the Society for the Prevention of Cruelty to Animals) this Pasteur Institute has received valuable assistance.

II. What should be done with the human being?

(a) Should he be treated, pending observation of the dog? or

(b) Should he await the results of the observation?

Lay before him the two courses and let him make his own choice. If he insists that you must decide, then, for self-protection, you must advise

treatment pending observation of the dog, which should be continued for 14 days; if the dog is well at the expiration of this period, tell the patient that the dog did not have rabies when he bit. That the saliva may be virulent 72 hours before symptoms appear is admitted; so if the dog shows symptoms on the fifteenth day his saliva may have been virulent on the twelfth day; most persons, notwithstanding your contrary opinion, would insist upon treatment. It is preferable for inoculation purposes to allow the dog to die; if killed early the medulla oblongata may not prove virulent.

If the dog has escaped, those bitten must be treated; so likewise, if the dog has been killed; if the dog is about to escape he should be killed for the protection of the public. All the early preliminary examinations have this deficiency: They may be negative and yet the animal may be rabid; they do not prove the negative, neither does animal inoculation when negative demonstrate that the virus may not have been previously present. For further reference of this point see " The Fallacy and Inutility of the So-called Rapid Diagnosis of Rabies " in a previous article.

ACCIDENTS PARALYTIQUES.

" Do you regard the paralysis as caused by the biting animal or by the fixed virus (of the treatment) ? Do you attribute it to a rabic toxin in the emulsion? " These questions were propounded by Dr. Remlinger, Director of the Pasteur Institute of Constantinople.

It is curious that several of the cases of paralysis were reported under the heading of " rabies cured by treatment," or of " rabies produced by treatment." In these conditions it has been stated, " there is no choking in swallowing water nor in draughts by fanning." It is contended that this disease, this paralysis, is not rabies, but a myelitis, which sometimes becomes ascending, reaching the medulla oblongata, and so causing death. This myelitis has been asserted to be the result of rabic toxin. Högyes, in 25,372 cases treated, has not had a case of paralysis; this has been ascribed to the very small amount of rabic toxin introduced in his method of treatment; very weak emulsion of the virulent medulla oblongata itself being used.

The occurrence of paralysis in connection with

the treatment is either accidental or incidental. Furthermore, it must be borne in mind that cold of itself is an efficient causative factor in producing myelitis, and was noted in seven of the cases collected by Remlinger.[1]

Observation XXII (Remlinger) is significant; this is the only case in which the demonstrative evidence of post-mortem examination was obtained:

A woman, 55 years of age, was bitten on the hand by a cat, from the brain of which it was not possible to produce rabies. Ten or twelve days after the bite, eight or ten days after the beginning of the treatment, after a period of two or three days of general malaise and pain in the back, she was seized with complete paralysis of the lower limbs; the arms, face, and sphincters were not involved. Death occurred in about a month. The autopsy by M. Chailloud revealed a "meningo-myelitis"; the cultures obtained furnished the pneumococcus (bacterium capsulatus lanceolatus). Cold is very favorable to the growth of this organism.[2]

Cases of paralysis of this character have been known to result from cold; such cases have lasted over periods of from 30 to 40 years, and were not recovered from.

Patients who undergo the Pasteur treatment have no immunity to infective myelitis of pneu-

[1] Annales de l'Institut Pasteur, Vol. XIX.

[2] Note the omission to inoculate from the medulla oblongata in this case.

mococcic or streptococcic origin; yet the only case in which post-mortem was made had as its lesion " meningo-myelitis," and as its organism the pneumococcus. It cannot be claimed that the pneumococcus is present in the anti-rabic or rabic material, as incidental thereto; therefore, if there at all, it must be accidental.

Had the bacillus of Dr. Bruschettini been found, the connection between the inoculated material and the disease would be of the nature of cause and effect.

The only other case resulting in death is the following:

OBSERVATION XX of M. Orlowski (see Remlinger). A woman of 48 years was bitten on the back of the hand; three weeks later, four days after the end of the treatment, she began to present paresis of the lower extremities; this increased little by little becoming a complete paraplegia; the paraplegia was accompanied by paralysis of the sphincters, paresis of the upper extremities, and uniform paralysis of the muscles of the face; this condition remained stationary for nine months, after which patient died under circumstances which were unfortunately little noted. For this reason this observation has no value.

The following case described as " paralytic rabies produced by the preventative inoculations " is of interest:

M. Gonzoles reports a case treated by the method of Ferran (of Barcelona) which presented paralysis of the limbs and

muscles of the face which recovered; he claims that "paralysis but rarely occurs in persons treated by this method (cords without drying or heating)." He adds: "A Spanish confrere cites the case of an officer suddenly smitten with a paraplegia on the last day of treatment; there is no further account of this case excepting that six years afterward the paraplegia had resisted all treatment." "Another case which developed on the last day of treatment was cured after six months by massage and electricity."

As "ascending paralysis supervening in the course of the treatment," the following case is cited:

OBSERVATION XI. A man 28 years of age, 23 days after having been bitten and five days after beginning the treatment, developed an ascending paralysis after taking a cold bath; complete recovery took place in two months.

The following case is given as one of "acute ascending paralysis supervening in the course of anti-rabic treatment":

OBSERVATION X. A servant, wounded while removing the pancreas of a man who had died of rabies on the eleventh day of treatment; in the course of his own anti-rabic treatment he developed the following symptoms: Fever, lumbar pains, incomplete paralysis of the lower extremities, and the sensation of tingling; the following day paralysis became complete, with anæsthesia from umbilical region down; there was retention of urine, and incontinence of feces; incomplete paralysis of the upper extremities then followed, preceded by tingling. The anti-rabic treatment was continued, the numbness diminished, vague movements reappeared in the legs, the paralysis of the bladder and rectum disappearing last; this condition lasted somewhat over a month. The almost constant existence of sphincter troubles is a very important argument against the hypothesis of hysteria.

In the following case the question arises as to whether "rabies may become ameliorated and recovery take place." It is Laveran's:

Observation I. A man of 22, neither alcoholic nor hysterical, was bitten in the left knee. Ten days later he began the anti-rabic treatment at Paris. For a week from the eighth day of treatment there were depression, insomnia, and sharp pains in the wound. Then the legs grew very feeble but were not completely paralyzed. There was displagia without dread of water. The anti-rabic treatment was discontinued; in a few days the symptoms diminished and disappeared. When recovery was complete, the treatment was resumed and finished without further accident.

As a case of "attenuated rabies very probably produced by anti-rabic inoculations," the following is given:

Observation II. A man, 42 years of age, was slightly bitten on the forearm, under circumstances which almost positively exclude rabies. One week after the accident he came to Paris and took the anti-rabic treatment for 17 days. The last two inoculations were followed by a condition of great lassitude, which increased the following day; three days after the end of the treatment general feebleness, insomnia, sensation of epigastric constriction, bilateral facial paralysis, with paralysis of the motor muscles of the eyes ensued; the lips and cheeks were paralyzed; the patient was unable to whistle, blow out, suck, or pronounce certain letters; the facial expression was lost; closing of the eyelids, moving of the wings of the nose were imperfect; myosis and diplopia existed; during the following days the general symptoms were ameliorated, but the paralytic phenomena persisted. It was only after a number of months that the paralytic symptoms receded. This patient presented no symptoms either of neurasthenia or of hysteria.

It may be inferred from the publications of Dr. Remlinger that in his opinion the Pasteur method should be discarded for the method of Högyes; when the *Institut Pasteur* of Paris shall do this, it will be obligatory on all similar institutions to do likewise.

In order to obtain the true nature of the " accidents paralytiques," saliva from these patients should be subdurally inoculated into rabbits and subjected to bacteriological examination and culture; the medulla oblongata of such as die should also be subdurally inoculated; the cerebro-spinal fluid from a lumbar puncture should likewise be investigated and subdurally inoculated.

" The existence of an intense lumbago with sensation of feebleness in the lower extremities permits us to foretell the appearance of paralysis."

" Stop the treatment and resume only when the symptoms are allayed;" " avoid all active medication and allow the disease to follow its natural tendency to cure." (Roux.)

Our institution in Baltimore has discontinued the use of emulsions of brain and medulla oblongata in ether, and no longer uses a cord that has been drying for three days. We use as

the strongest cord one that has been drying four days. All cords are hung in the vessel close over the caustic potash and *no moist cord is used.* It may be that all virulent cords could be excluded without disadvantage.

It is remarkable that almost without exception persons undergoing treatment have improved in general health. A gentleman bitten by a cat, presenting himself for treatment, was assured the cat was not mad. He then asked if persons undergoing Pasteur treatment improved in general health, and on being told that they did, stating that his general health had been bad for some time, he insisted on taking the treatment. He was treated and subsequently informed us that he had never enjoyed better health.

In conclusion it is important as well as interesting to learn from the statistics of Remlinger (herewith printed) that the 22 cases of "accidents paralytiques," including the two fatal cases described, occurred in about 60,000 patients treated at various institutions. While in over 100,000 collected in the second table there was not a single accident of the kind reported:

Institute.	Author.	Number of patients.	Cases.	Days after bite.	Days after beginning treatment.
Paris.	Chailloud.	9,074	2	12 10 or 12	11 8 or 10
St. Petersburg.	Kraïouchkine.	7,253	1	19	16
Palerme.	de Blasi.	7,129	4	28 30 35 12	21 8 Day after end of treatm 8
Algiers.	Soulié.	4,755	1	28	Paralysis began on 5th d was complete on the 14t
Naples.	Calabrese.	4,578	2	? 17	10 13
Constantinople.	Remlinger.	3,291	1	18	12
Bologna.	Ivo Novi.	3,067	5	88 25 20 51 28	14 Last day of treatmen 14 12 17
Milan.	Segré.	2,942	1	26	15
Wilna.	Orlowski.	2,900	2	21 21	4 days after end of treat 1 week after end of treat
Jassy.	Lebell.	2,850	7	10 to 18	8 to 11
Faenza.	Baschieri.	1,440	1	16	8
Turin.	Bordoni-Uffreduzzi.	?	2	24 20	Day after end of treatm 4 days after end of treat
Florence.	Daddi.	?	1	28	13
13 institutions	. . . . .	50,280	30		

* Afterw

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Institute.	Author.	Number of patients.	Cases.	Institute.	A
Budapest.	Högyes.	25,372	0	Montpellier.	Rodet
Lisbon.	Bettencourt.	7,479	0	Lille.	Calm
Athens.	Pamponkis.	4,045	0	Rome.	Marir
Cracovie.	Bujwid.	3,800	0	Tunis.	C. Ni
Marseilles.	Livor.	3,563	0	Bordeaux.	Ferré
Kasauli.	Semple.	2,407	0	Vienna.	Paltau

Total number of patients in 30 institutions, 108,712. Total number of cases in 30 institutions, 30.

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E I.

Nature of paralysis.	Duration.	Termination.
Lower and upper extremities and sphincters.	20 days.	Recovery.
Lower extremities.	1 month.	Death.
Lower extremities and sphincters.	10 days.	Recovery.
Lower extremities, muscles of face and sphincters.	9 days.	Recovery.
Lower extremities and sphincters.	20 days.	Recovery.
Lower extremities, sphincters and muscles of face.	8 days.	Recovery.
Lower extremities and sphincters.	20 days.	Recovery.
Lower extremities and sphincters.	1 month.	Recovery.
Lower extremities and sphincters.	5	Recovery.
Lower extremities and sphincters.	?	Recovery.
Lower and upper extremities, sphincters and muscles of the face.	1 month.	Recovery.
Lower extremities, orbicularis oris.	20 days.	Recovery.
Lower extremities, sphincters.	10 days.	Recovery.
Lower extremities.	?	Improvement.*
Lower extremities.	?	Recovery.
Lower extremities and sphincters,	?	Recovery.
Lower extremities and sphincters.	8 days.	Recovery.
Lower extremities, sphincters, upper extremities, muscles of face.	9 months.	Death.
Lower extremities, sphincters, upper extremities, muscles of face.	A few months.	Recovery.
Lower extremities, sphincters and upper extremities.	8 to 10 days.	Recovery.
Lower extremities.	1 week.	Recovery.
Lower extremities and sphincters.	15 days.	Recovery.
Lower extremities, sphincters and upper extremities.	Several months.	Recovery.
Lower extremities and sphincters.	15 days.	Recovery.

t sight of.

l II.

	Number of patients.	Cases.	Institute.	Author.	Number of patients.	Cases.
	2,201	0	Le Caire.	Tonin.	1,000	0
	2,160	0	Saigon.	Calmette.	600	0
.	1.940	0	Madrid.	Murillo.	500	0
	1,690	0	Sassari.	?	?	0
	1,350	0	Shangaï.	Moore.	?	0
	1,326	0				
			17 institutions	. . . . .	58,432	0

APPENDIX.[1]

I.

Cure of a Case of Rabies in Man.

Peter Ciornei, age six years, was brought to the institute at Jassy on August 26th, 1894. The child had been bitten by a dog suspected of having rabies; that it was rabies was later proven at the institute.

The child bore two marks of teeth in the right temporal region; upon the back of the right hand there were four other imprints—two deep and through the whole thickness of the skin, and three more tooth marks upon the external aspect of the left forearm. These last tore the shirt.

From August 26th to September 11th, 1894, the following treatment was administered to the child:

Date.	Quantity. grams	Cords of. days
August 26, 1894.....	3	12, 11, 10, 9
" 27, "	3	8, 7, 6
" 28, "	3	6, 5, 4[1]
" 29, "	3	4, 3, 2[1]
" 30, "	3	2, 1[1]
" 31, "	3	1, 0[1]

[1] The cords of the 4, 3, 2, 1 and 0 days are in emulsions heated to 80° C. In all 24 grams of emulsion were given. 80° C. = 176° F. A temperature of 118° F. destroys the rabic virus.

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[1] See Annales de l'Institut Pasteur.

Date.			Quantity. grams	Cords of. days
September	1,	1894	3	12, 11
"	2,	"	3	9, 8
"	3,	"	3	7, 6
"	4,	"	3	5, 4[2]
"	5,	"	3	3, 2[2]
"	6,	"	3	1, 0[2]
"	7,	"	3	8, 6
"	8,	"	3	5, 4[2]
"	9,	"	3	3, 2[2]
"	10,	"	3	2, 1[2]
"	11,	"	3	1, 0[2]

[2] Emulsions heated to 80° C. In all 42 grams were given. 80° C. = 176° F.

On September 11th, 1894, treatment was suspended because the child was seriously ill.

As a matter of fact, on September 9th, there appeared symptoms of restlessness; at the evening inoculation the child was pale and depressed.

On September 10th the depression persisted, the eyes were dull and without expression. During the night of September 10th the child was agitated, it had convulsions. About midnight the temperature arose to 39.4° C (102.9° F.) and the pulse to 80.

At 11 a. m., September 11th, 1894, the child was pale and feeble; the appetite failed and it drank water with difficulty.

At 5 p. m., on September 11th, pulse is 78, and is irregular and feeble; respiration irregular

and 42 per minute; hydrophobia and aërophobia pronounced; slight cyanosis of the lips. Extremities cold.

September 11th, 1894, at 11 p. m., on a visit to the patient at the hospital, we found it in very violent tonic and clonic convulsions, which were general; the injic eyes are half shut, respiration very difficult and very frequent—56 per minute—pulse imperceptible, trachial râles.

At 9 a. m., on September 12th, there was marked prostration; more convulsions; during the night the child vomited twice; pulse 72, with few intermissions, perceptibly stronger; temperature, 99.5° F., hydrophobia less pronounced.

9 a. m., September 13th: Aside from the general weakness, all the alarming symptoms are better; the child grew better from day to day until September 20th, when it was returned to the institute, when the interrupted treatment was completed as follows:

Date.	Quantity. grams	Cords of. days
September 21, 1894.....	3	10, 9
" 22, "	3	8, 7
" 23, "	3	6, 5
" 24, "	3	5, 4
" 25, "	3	4
" 26, "	3	3
" 27, "	3	3
" 28, "	3	2
" 29, "	3	2

The cords used from the 24th to the 29th of September are all prepared from the fixed virus heated to 80° C. Here are 21 grams more.

In all, the child had therefore received, in addition to the cords given according to the Pasteur method, 87 grams of emulsion of the fixed virus sterilized at 80° C., which is equal to three-fourths of a rabbit's brain. The little patient recovered and thereafter remained well.

II.

Lina Luzzani found typical Negri bodies in a normal cat. Pacé found corpuscles identical with Negri bodies in the brains of three persons, one dead of old age, one of cerebral embolism and one of aortic insufficiency. Babes found Negri bodies in the spinal ganglia in a case of death from arsenical poisoning. See " L'Étude expérimentale de la Rage," by Marie, 1909.

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